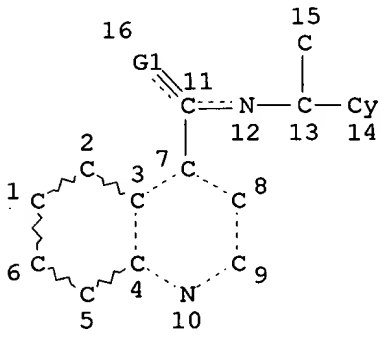
=> fil marpat; d que stat
FILE 'MARPAT' ENTERED AT 10:37:02 ON 20 JUN 1997
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE CONTENT: 1988-PRESENT (VOL 104 ISS 14-VOL 126 ISS 24) (970613/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	5629460	13 MAY 1997
DE	19540360	7 MAY 1997
EP	773212	14 MAY 1997
JP	09068701	11 MAR 1997
WO	9713756	17 APR 1997

L1 STR



VAR G1=O/S/N
NODE ATTRIBUTES:
NSPEC IS RC AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

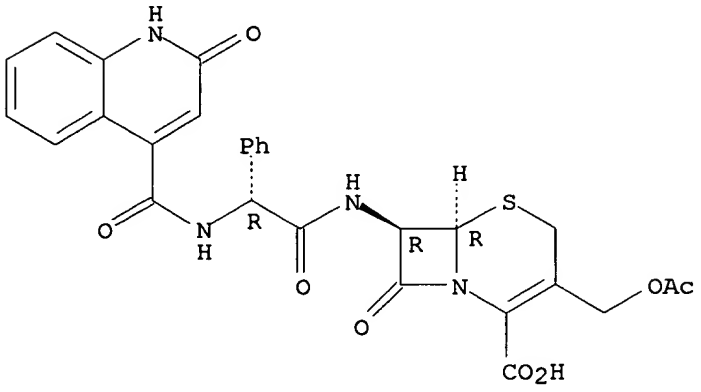
ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L3 34 SEA FILE=MARPAT SSS FUL L1 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 7224 ITERATIONS 34 ANSWERS
SEARCH TIME: 00.01.58

quinolinyl)carbonyl]amino]phenylacetyl]amino]-8-oxo-,
[6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



FILE 'MARPAT' ENTERED AT 11:17:00 ON 17 JUN 1997
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

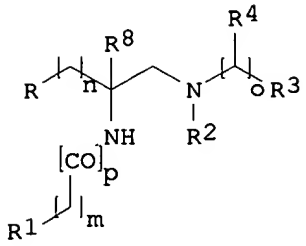
FILE CONTENT: 1988-PRESENT (VOL 104 ISS 14-VOL 126 ISS 24) (970613/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

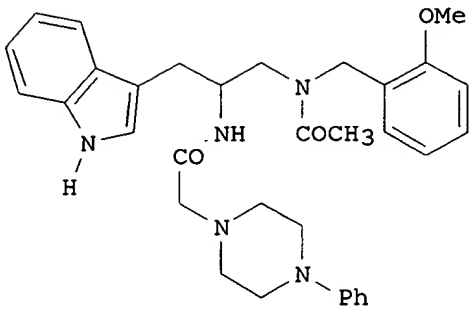
US	5629460	13 MAY 1997
DE	19540360	7 MAY 1997
EP	773212	14 MAY 1997
JP	09068701	11 MAR 1997
WO	9713756	17 APR 1997

=> d 1-34 .bevmar; fil marpatprev

L17 ANSWER 1 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 126:277498 MARPAT
TI Preparation of 2-piperazino(or piperidino)acetylaminopropanamines as growth hormone secretagogues
IN Dodge, Jeffrey Alan; Hipskind, Philip Arthur
PA Lilly, Eli, and Co., USA
SO Eur. Pat. Appl., 107 pp.
CODEN: EPXXDW
PI EP 761219 A1 970312
DS R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
AI EP 96-305917 960814
PRAI US 95-2581 950821
DT Patent
LA English
GI



I



II

AB The title compds. [I; m, n, p = 0-1; o = 0-2; R = Ph, 2-indolyl, benzothienyl, etc.; R1 = Ph3C, Ph, Ph2CH, etc.; R2 = H, C1-4 alkyl, arylsulfonyl, etc.; R3 = Ph, naphthyl, C1-8 alkyl, etc.; R4 = H, C1-3 alkyl; R8 = H, C1-6 alkyl], useful in treating a physiol. condition which may be modulated by an increase in growth hormone, were prepd. and formulated. Thus, treatment of 2-[(4-phenyl)piperazin-1-yl]acetic acid sodium salt with Et3N.HBr and carbonyldiimidazole in DMF followed by addn. of 2-amino-3-(1H-indol-3-yl)-1-[N-(2-methoxybenzyl)amino]propane in DMF afforded the title compd. II. Compds. I are effective at 1-15 mg/kg/day. This invention also provides methods for the treatment of such physiol. conditions which comprise administering a growth hormone secretagogue as described in the present invention in combination with growth hormone releasing hormone.

IC ICM A61K031-445
ICS A61K031-495

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 2, 34, 63

ST growth hormone secretagogue piperazinoacetylaminopropanamine piperidinoacetylaminopropanamine prepn

IT 170508-05-1P 170566-34-4P 170566-35-5P 170566-36-6P
170566-37-7P 170566-38-8P 170566-39-9P 170566-40-2P
170566-41-3P 170566-42-4P 170566-43-5P 170566-44-6P
170566-45-7P 170566-46-8P 170566-47-9P 170566-48-0P
170566-49-1P 170566-50-4P 170566-51-5P 170566-52-6P
170566-53-7P 170566-54-8P 170566-55-9P 170566-56-0P
170566-57-1P 170566-58-2P 170566-59-3P 170566-60-6P
170566-61-7P 170566-62-8P 170566-63-9P 170566-64-0P
170566-65-1P 170566-66-2P 170566-67-3P 170566-68-4P
170566-69-5P 170566-70-8P 170566-71-9P 170566-72-0P
170566-73-1P 170566-74-2P 170566-75-3P 170566-76-4P
170566-77-5P 170566-78-6P 170566-79-7P 170566-80-0P
170566-81-1P 170566-82-2P 170566-83-3P 170566-84-4P

170566-85-5P 170566-86-6P 170566-87-7P 170566-88-8P
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170566-99-1P 170567-00-7P 170567-01-8P 170567-02-9P
170567-03-0P 170567-04-1P 170567-06-3P 170567-07-4P
170567-08-5P 170567-09-6P 170567-10-9P 170567-11-0P
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170567-28-9P 170567-29-0P 170567-30-3P 170567-31-4P
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170567-42-7P 170567-43-8P 170567-44-9P 170567-45-0P
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170567-54-1P 170567-55-2P 170567-56-3P 170567-57-4P
170567-58-5P 170567-59-6P 170567-60-9P 170567-61-0P
170567-62-1P 170567-63-2P 170567-64-3P 170567-65-4P
170567-66-5P 170567-67-6P 170567-68-7P 170567-69-8P
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170567-82-5P 170567-83-6P 170567-84-7P 170567-85-8P
170567-86-9P 170567-87-0P 170567-88-1P 170567-89-2P
170567-90-5P 170567-91-6P 170567-92-7P 170567-93-8P
170567-94-9P 170567-95-0P 170567-96-1P 170567-97-2P
170567-98-3P 170567-99-4P 170568-00-0P 170568-01-1P
170568-05-5P 170568-06-6P 170568-07-7P 170568-08-8P
170568-09-9P 170568-10-2P 170568-26-0P 170568-27-1P
170568-28-2P 170568-29-3P 188949-03-3P 188949-04-4P
188949-05-5P 188949-06-6P 188949-07-7P 188949-08-8P
188949-09-9P 188949-10-2P 188949-11-3P 188949-17-9P
188949-19-1P 188949-21-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-piperazino(or piperidino)acetylaminopropanamines as growth hormone secretagogues)

IT 9002-72-6, Growth hormone
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of 2-piperazino(or piperidino)acetylaminopropanamines as growth hormone secretagogues)

IT 76-83-5, Trityl chloride 89-98-5, 2-Chlorobenzaldehyde 96-32-2, Methyl bromoacetate 109-02-4, N-Methylmorpholine 135-02-4, 2-Methoxybenzaldehyde 153-94-6, D-Tryptophan 541-41-3, Ethyl chloroformate 4897-50-1, 4-(Piperidin-1-yl)piperidine 6850-57-3, 2-Methoxybenzylamine 7303-48-2, DL-Tryptophanamide 17766-28-8, 1-Cyclohexylpiperazine 24424-99-5, Di-tert-butyl dicarbonate 119378-70-0 188943-14-8 188949-25-9
RL: RCT (Reactant)
(prepn. of 2-piperazino(or piperidino)acetylaminopropanamines as growth hormone secretagogues)

IT 170508-01-7P 170568-11-3P 170568-12-4P 170568-13-5P
170568-14-6P 170568-15-7P 170568-16-8P 170568-17-9P
170568-18-0P 170568-19-1P 170568-21-5P 170568-22-6P
170568-32-8P 174225-59-3P 174634-02-7P 174634-03-8P
174634-04-9P 175460-96-5P 175460-97-6P 175460-99-8P
188943-09-1P 188949-23-7P 188949-24-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of 2-piperazino(or piperidino)acetylaminopropanamines as growth hormone secretagogues)

L17 ANSWER 2 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 126:225557 MARPAT
TI Acylated oligopeptides containing phosphotyrosine as inhibitors of protein tyrosine kinases
IN Garcia-Echeverria, Carlos; Gay, Brigitte; Furet, Pascal
PA Ciba-Geigy A.-G., Switz.; Garcia-Echeverria, Carlos; Gay, Brigitte; Furet, Pascal
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
PI WO 9707131 A1 970227
DS W: AL, AU, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 96-EP3479 960806
PRAI GB 95-16842 950817
DT Patent
LA English
AB Peptides R-A-B-PTI-(AA)m-R1 (R = aryl-, cycloalkyl-, or heterocyclylcarbonyl or -sulfonyl; R1 = OH, C-terminal protecting group, or primary, secondary, or tertiary amino group; A is absent or bivalent radical of natural or unnatural amino acid; B = bivalent radical of natural amino acid; PTI = bivalent radical of phosphotyrosine or phosphotyrosine mimic; AA = bivalent radical of natural or unnatural amino acid; m = 2-15), as well as their intramol. disulfide derivs. and salts, were prepd. as inhibitors or protein tyrosine kinases. Thus, 2-aminobenzoyl-Glu-Tyr(PO3H2)-Ile-Asn-Gln-NH2 trifluoroacetate salt was prepd. by the solid phase method and had an IC50 value of 0.022 .mu.M in a test system using the phosphorylated "tail" EGFR-MBP fusion protein as ligand. Formulations contg. acylated oligopeptides are described.
IC ICM C07K007-02
ICS C07K007-06; A61K038-08
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7, 63
ST phosphotyrosyl peptide prepn inhibitor tyrosine kinase
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylated oligopeptides contg. phosphotyrosine as inhibitors of protein tyrosine kinases)
IT 188293-97-2P 188294-15-7P 188294-17-9P 188294-19-1P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylated oligopeptides contg. phosphotyrosine as inhibitors of protein tyrosine kinases)
IT 188293-78-9P 188293-79-0P 188293-84-7P 188293-88-1P
188293-89-2P 188293-94-9P 188293-96-1P 188293-99-4P
188294-00-0P 188294-01-1P 188294-03-3P 188294-04-4P
188294-06-6P 188294-07-7P 188294-08-8P 188294-09-9P
188294-11-3P 188294-12-4P 188294-13-5P 188294-14-6P
188294-18-0P 188294-20-4P 188294-21-5P 188294-22-6P
188294-23-7P 188294-24-8P 188294-25-9P 188294-26-0P
188294-27-1P 188294-28-2P 188294-29-3P 188294-30-6P

188294-31-7P 188294-33-9P 188294-34-0P 188294-35-1P
188294-36-2P 188294-37-3P 188294-38-4P 188294-39-5P
188294-40-8P 188294-41-9P 188294-42-0P 188294-43-1P
188294-44-2P 188294-45-3P 188294-46-4P 188294-47-5P
188294-48-6P 188294-49-7P 188294-50-0P 188294-52-2P
188294-54-4P 188294-55-5P 188294-57-7P 188294-59-9P
188294-60-2P 188294-61-3P 188294-62-4P 188294-63-5P
188294-64-6P 188294-65-7P 188294-66-8P 188294-67-9P
188294-68-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylated oligopeptides contg. phosphotyrosine as inhibitors of protein tyrosine kinases)

IT 80449-02-1, Protein tyrosine kinase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of acylated oligopeptides contg. phosphotyrosine as inhibitors of protein tyrosine kinases)

IT 93-10-7, 2-Quinolinecarboxylic acid 99-05-8, 3-Aminobenzoic acid 99-06-9, 3-Hydroxybenzoic acid, reactions 100-09-4, 4-Methoxybenzoic acid 118-92-3, 2-Aminobenzoic acid 486-73-7, 1-Isoquinolinecarboxylic acid 535-87-5, 3,5-Diaminobenzoic acid 605-65-2, Dansyl chloride 771-50-6, 3-Indolecarboxylic acid 1477-50-5, 2-Indolecarboxylic acid 2756-85-6 5345-47-1, 2-Aminonicotinic acid 5424-01-1, 3-Amino-2-Pyrazinecarboxylic acid 5959-52-4, 3-Amino-2-naphthoic acid 6480-68-8, 3-Quinolinecarboxylic acid 18704-37-5, 8-Quinolinesulfonyl chloride 78348-24-0, 2-Indolinecarboxylic acid 86060-81-3 147762-53-6 156017-45-7
RL: RCT (Reactant)
(prepn. of acylated oligopeptides contg. phosphotyrosine as inhibitors of protein tyrosine kinases)

IT 66493-39-8P 111331-82-9P 115951-16-1P 117322-30-2P 162648-54-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of acylated oligopeptides contg. phosphotyrosine as inhibitors of protein tyrosine kinases)

L17 ANSWER 3 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 126:190949 MARPAT
TI Use of a tachykinin antagonist and a muscarinic antagonist and/or an antihistamine to treat motion sickness
IN Tattersall, Frederick David
PA Merck Sharp & Dohme Limited, UK; Tattersall, Frederick David
SO PCT Int. Appl., 131 pp.
CODEN: PIXXD2
PI WO 9702824 A1 970130
DS W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 96-GB1628 960708
PRAI GB 95-13972 950708
DT Patent
LA English
AB The present invention relates to the use of a tachykinin antagonist and a muscarinic antagonist and/or an antihistamine for manuf. of a

medicament for the treatment or prevention of motion sickness. There is also provided pharmaceutical compns. and products comprising a tachykinin antagonist and a muscarinic antagonist and/or an antihistamine. Examples of prepn. of tachykinin antagonists were given, e.g., 2-(R)-[1-(R)-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(S)-(4-fluorophenyl)-4-[3-(5-oxo-1,2,4-triazolo)methyl]morpholine.

IC ICM A61K031-535
ICS A61K031-66; A61K031-40; A61K031-14; A61K031-445

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 28

ST motion sickness tachykinin muscarinic antagonist antihistaminic

IT Tachykinins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; tachykinin antagonist and muscarinic antagonist and/or antihistaminic to treat motion sickness)

IT Antiemetics
Antihistamines
Motion sickness
Muscarinic antagonists
(tachykinin antagonist and muscarinic antagonist and/or antihistaminic to treat motion sickness)

IT 100-52-7, Benzaldehyde, reactions 106-96-7, Propargyl bromide 405-50-5, 4-Fluorophenylacetic acid 785-56-8, 3,5-Bis(trifluoromethyl)benzoyl chloride 821-10-3, 1,4-Dichloro-2-butyne 1271-19-8, Titanocene dichloride 90719-32-7, (S)-4-Benzyl-2-oxazolidinone 155742-64-6
RL: RCT (Reactant)
(tachykinin antagonist and muscarinic antagonist and/or antihistaminic to treat motion sickness)

IT 79-44-7P, N,N-Dimethylcarbamoyl chloride 459-04-1P, 4-Fluorophenylacetyl chloride 1271-66-5P, Dimethyl titanocene 19883-57-9P, (S)-4-Fluorophenylglycine 24843-91-2P 42718-13-8P 71783-54-5P 159706-87-3P 159707-16-1P 159707-17-2P 159707-18-3P 170729-77-8P 170729-78-9P 170902-74-6P 170902-75-7P 171242-24-3P 171242-93-6P 171243-11-1P 171243-12-2P 171243-15-5P 171338-27-5P 171482-05-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(tachykinin antagonist and muscarinic antagonist and/or antihistaminic to treat motion sickness)

IT 170729-80-3P 171242-15-2P 171243-13-3P 171243-14-4P 172822-02-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin antagonist and muscarinic antagonist and/or antihistaminic to treat motion sickness)

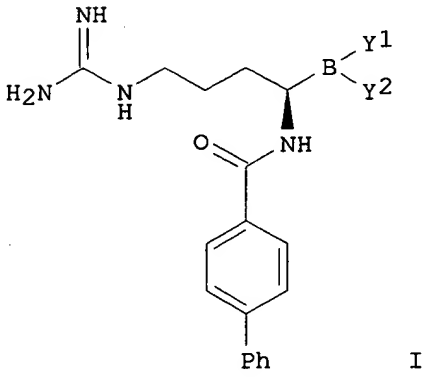
IT 51-34-3, Scopolamine 58-38-8, Prochlorperazine 58-39-9, Perphenazine 58-73-1, Diphenhydramine 60-87-7, Promethazine 60-99-1, Methotrimeprazine 82-92-8, Cyclizine 82-93-9, Chlorcyclizine 82-95-1, Buclizine 86-21-5, Pheniramine 117-89-5, Trifluoperazine 298-57-7, Cinnarizine 362-29-8, Propiomazine 523-87-5, Dimenhydrinate 569-65-3, Meclozine 604-73-9, Chlorpromethazine 52468-60-7, Flunarizine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin antagonist and muscarinic antagonist and/or antihistaminic to treat motion sickness)

L17 ANSWER 4 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 126:89156 MARPAT
TI Preparation of chiral isothioyanates as derivatizing agents

IN Lindner, Wolfgang; Kleidernigg, Oliver Paul
PA Lindner, Wolfgang, Austria; Kleidernigg, Oliver Paul
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
PI WO 9637465 A1 961128
DS W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 96-EP2258 960524
PRAI EP 95-108125 950526
DT Patent
LA English
AB R1NHCHR2CHR3NCS [R1 = COR4, CO2R5, SO2R6; R2,R3 = aliph. or arom. group; R2R3 = atoms to complete carbocyclic or heterocyclic ring; R4 = aliph. or (hetero)arom. group, aralkyl; R5 = CMe3, (nitro)benzyl, fluorenylmethyl; R6 = (hetero)aryl] were prepd. Thus, (R,R)-1,2-diaminocyclohexane was cyclocondensed with CS2 and the product amidated by 3,5-(O2N)2C6H3COCl to give (R,R)-N-(2-isothiocyanatocyclohexyl)-3,5-dinitrobenzamide. The latter was used to prep. diastereomeric derivs. of (R)-, and (S)-propranolol. Data for chromatog. sepns. of, e.g., amino acids, etc. were given.
IC ICM C07C331-24
ICS C07C331-26; C07D215-50; C07B057-00
CC 25-22 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 9
ST chiral isothiocyanate prepn derivatizing agent
IT Chromatography
(electro-; prepn. of chiral isothiocyanates as derivatizing agents)
IT Liquid chromatographic chiral stationary phases
(prepn. of chiral isothiocyanates as derivatizing agents)
IT 167771-21-3P 177697-35-7P 185508-68-3P 185508-69-4P
185508-71-8P 185508-72-9P 185508-73-0P 185508-74-1P
185508-84-3P 185508-85-4P 185508-86-5P 185508-87-6P
185508-89-8P 185508-91-2P 185508-92-3P 185508-94-5P
185508-96-7P
RL: NUU (Nonbiological use, unclassified); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(prepn. of chiral isothiocyanates as derivatizing agents)
IT 185509-02-8P 185509-04-0P 185509-05-1P 185509-07-3P
RL: PUR (Purification or recovery); PREP (Preparation)
(prepn. of chiral isothiocyanates as derivatizing agents)
IT 185508-76-3P 185509-00-6P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of chiral isothiocyanates as derivatizing agents)
IT 99-33-2, 3,5-Dinitrobenzoyl chloride 106-95-6, Allyl bromide, reactions 3282-30-2, Pivaloyl chloride 4199-09-1, (S)-Propranolol 5051-22-9, (R)-Propranolol 5132-80-9, 9-Acridinecarbonyl chloride hydrochloride 13013-17-7 13822-56-5, 3-Aminopropyltrimethoxysilane 20439-47-8, (R,R)-1,2-Diaminocyclohexane 21436-03-3, (S,S)-1,2-Diaminocyclohexane 38460-95-6, 10-Undecenoyl chloride 185508-83-2
RL: RCT (Reactant)
(prepn. of chiral isothiocyanates as derivatizing agents)
IT 139237-77-7P 185508-82-1P 185508-98-9P 185546-54-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of chiral isothiocyanates as derivatizing agents)
IT 185508-78-5P 185508-79-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of chiral isothiocyanates as derivatizing agents)

L17 ANSWER 5 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 126:31466 MARPAT
TI Boronic acid and ester inhibitors of thrombin
IN Amparo, Eugene C.; Miller, William H.; Pacofsky, Gregory J.; Wityak, John; Weber, Patricia C.; Duncia, John J. V.; Santella, Iii Joseph B.
PA The Dupont Merck Pharmaceutical Company, USA
SO U.S., 170 pp. Cont.-in-part of U.S. Ser. No. 348,029.
CODEN: USXXAM
PI US 5563127 A 961008
AI US 94-364338 941227
PRAI US 93-36377 930324
US 94-318029 941004
US 94-348029 941201
DT Patent
LA English
GI



I

AB Novel boronic acid and ester and carboxyl-modified amino acid compds. R1-Z-CHR2-A (A = organoboryl, BY1Y2; Y1, Y2 = independently OH, F, organoamino, C1-8 alkoxy, Y1Y2 = cyclic boron ester, amide contg. N, S, O; etc.; Z = (CH2)mCX, X = amido, thioamido, etc., substituted C1-12 alkyl, alkenyl, etc.; R1 = arylalkenyl, aryl = substituted Ph, naphthyl, biphenyl, etc.; R2 = substituted C1-12 alkyl, alkenyl, etc.), which are inhibitors of trypsin-like enzymes, are disclosed. Thus, amino acid modified boronic ester I (Y1Y2 = (+)-pinanediol) was prepd. in multiple steps starting from (+)-pinanediol 4-bromo-1(R)-(4-phenylbenzoyl)aminobutane-1-boronate. Thrombin inhibition activity of some of the compds. prepd. is described.
IC ICM A61K031-395
ICS C07D249-08
NCL 514064000
CC 29-4 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1
ST amino acid boronate ester inhibitor thrombin

IT 180896-93-9P 180897-02-3P 180897-04-5P 180897-05-6P
180897-06-7P 180897-07-8P 180897-08-9P 180897-09-0P
180897-11-4P 180897-12-5P 180897-13-6P 180897-14-7P
180897-15-8P 180897-16-9P 180897-17-0P 180897-18-1P
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180897-25-0P 180897-26-1P 180897-27-2P 180897-28-3P
180897-29-4P 180897-30-7P 180897-31-8P 180897-32-9P
180897-33-0P 180897-34-1P 180897-35-2P 180897-36-3P
180897-37-4P 180897-38-5P 180897-39-6P 180897-40-9P
180897-41-0P 180897-42-1P 180897-43-2P 180897-44-3P
180897-45-4P 180897-46-5P 180897-47-6P 180897-48-7P
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180897-53-4P 180897-55-6P 180897-56-7P 180897-57-8P
180897-58-9P 180897-59-0P 180897-60-3P 180897-61-4P
180897-62-5P 180897-63-6P 180897-64-7P 180897-65-8P
180897-66-9P 180897-68-1P 180897-69-2P 180897-71-6P
180897-72-7P 180897-73-8P 180897-74-9P 180897-75-0P
180897-76-1P 180897-77-2P 180897-78-3P 180897-79-4P
180897-80-7P 180897-81-8P 180897-82-9P 180897-83-0P
180897-84-1P 181138-50-1P 181138-51-2P 181138-52-3P
181138-53-4P 181138-54-5P 181138-55-6P 181138-56-7P
181138-57-8P 181138-58-9P 181138-68-1P 181138-70-5P
181138-71-6P 181138-72-7P 181138-73-8P 181138-76-1P
181138-77-2P 181138-78-3P 181138-79-4P 181138-80-7P
181138-81-8P 181138-82-9P 181138-83-0P 181138-84-1P
181138-85-2P 181138-86-3P 181138-87-4P 181138-88-5P
181138-89-6P 181138-90-9P 181138-91-0P 181227-38-3P
183791-98-2P 183791-99-3P 183792-03-2P 183904-56-5P
183904-57-6P 183904-58-7P 183904-59-8P 183904-60-1P
183904-61-2P 183904-62-3P 183904-63-4P 183904-64-5P
183904-65-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid-modified boronic acids and esters as inhibitors of thrombin)

IT 9002-04-4, Thrombin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of amino acid-modified boronic acids and esters as inhibitors of thrombin)

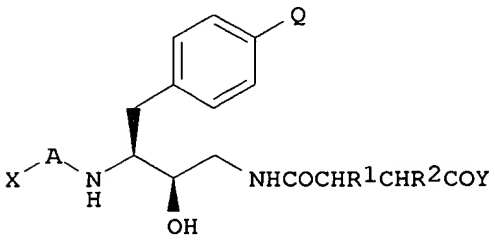
IT 62-56-6, Thiourea, reactions 140-29-4, Phenylacetonitrile
140-87-4, Cyanoacetohydrazide 868-59-7, Cysteine ethyl ester hydrochloride 13226-93-2 14002-51-8, 4-Phenylbenzoyl chloride
131100-00-0 165881-38-9
RL: RCT (Reactant)
(prepn. of amino acid-modified boronic acids and esters as inhibitors of thrombin)

IT 5442-34-2P 57723-86-1P 103249-79-2P 180896-85-9P
180896-88-2P 180896-89-3P 180896-90-6P 180896-91-7P
180896-94-0P 180896-96-2P 180896-99-5P 180897-01-2P
181033-28-3P 181033-29-4P 181033-30-7P 181138-47-6P
181138-48-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of amino acid-modified boronic acids and esters as inhibitors of thrombin)

IT 180896-86-0P 180896-92-8P 180896-95-1P 181138-49-8P
181139-17-3P 181227-37-2P 184046-16-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of amino acid-modified boronic acids and esters as

inhibitors of thrombin)

L17 ANSWER 6 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 125:222433 MARPAT
TI HIV protease-inhibiting succinic acid 1,3(S)-diamino-4-phenyl-2(R)-butanol derivatives
IN Beaulieu, Pierre L.; Guse, Ingrid
PA Bio-Mega/boehringer Ingeleheim Research Inc., Can.
SO U.S., 14 pp.
CODEN: USXXAM
PI US 5545640 A 960813
AI US 95-416239 950404
DT Patent
LA English
GI



I

AB Disclosed herein are compds. which inhibit human immunodeficiency virus (HIV) protease activity and inhibit HIV replication in human cells. Thus, the compds. are indicated for the treatment of HIV infections. The compds. can be represented by the formula I wherein X is a terminal group, for example, an aryloxycarbonyl, an alkanoyl or an arylalkyl carbamoyl; A is absent or an amino acid or a derived amino acid; either R1 or R2 is hydrogen while the other is alkyl or R1 and R2 are joined to form a cyclohexane; Q is hydrogen, hydroxy, halo or lower alkoxy; and Y is a terminal group, for example, an alkylamino, alkoxy or an optionally substituted anilino. Thus, e.g., amide coupling of 1-amino-3(S)-(dibenzylamino)-4-phenyl-2(R)-butanol with 4-(1-ethylpropylamino)-2(R)-tert-butyl-4-oxobutanoic acid (both prepd.) provided N4-[3(S)-(dibenzylamino)-2(R)-hydroxy-4-phenylbutyl]-N1-(1-ethylpropyl)-3(R)-tert-butylbutanediamide; deprotection to the 3(S) amino deriv. followed by coupling with N-Boc-Thr-OH, deprotection, and coupling with 2-quinolinecarboxylic acid afforded I [X = 2-quinolinecarbonyl, A = Thr, Q = H, R1 = (R)-tert-Bu, R2 = H, Y = NHCHEt2] which exhibited IC50 = 4 nM for inhibition of HIV protease and EC50 = 52 nM for inhibition of syncytia formation.
IC ICM C07D215-48
ICS C07C271-20; A61K031-47
NCL 514311000
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
ST succinate diaminophenylbutanol deriv HIV protease inhibitor
IT Acquired immune deficiency syndrome
(treatment; HIV protease inhibiting succinic acid 1,3(S)-diamino-4-phenyl-2(R)-butanol derivs.)
IT 181038-55-1P 181038-58-4P 181038-62-0P 181038-65-3P
181038-69-7P 181038-72-2P 181038-74-4P 181038-76-6P

181038-79-9P 181038-82-4P 181038-85-7P 181038-87-9P
181038-89-1P 181038-92-6P 181038-95-9P 181038-97-1P
181038-99-3P 181039-01-0P 181039-03-2P 181039-06-5P
181039-07-6P 181039-08-7P 181039-10-1P 181039-11-2P
181039-12-3P 181039-13-4P 181039-14-5P 181039-15-6P
181039-16-7P 181039-17-8P 181039-20-3P 181039-21-4P
181039-22-5P 181039-24-7P 181039-26-9P 181039-28-1P
181039-30-5P 181039-32-7P 181039-34-9P 181039-36-1P
181039-39-4P 181039-41-8P 181039-43-0P 181039-47-4P
181039-50-9P 181039-52-1P 181039-53-2P 181039-55-4P
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181039-90-7P 181039-92-9P 181039-94-1P 181039-96-3P
181039-98-5P 181040-00-6P 181040-02-8P 181040-03-9P
181040-05-1P 181229-35-6P 181229-36-7P 181229-37-8P
181229-38-9P 181229-39-0P 181229-40-3P 181229-41-4P
181229-42-5P 181229-43-6P 181229-44-7P 181229-45-8P
181229-46-9P 181229-47-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HIV protease inhibiting succinic acid 1,3(S)-diamino-4-phenyl-2(R)-butanol derivs.)

IT 93-10-7, 2-Quinolinecarboxylic acid 105-36-2, Ethyl bromoacetate 576-26-1, 2,6-Dimethylphenol 616-24-0, 1-Ethylpropylamine 2592-18-9 117237-87-3 118970-37-9
RL: RCT (Reactant)
(HIV protease inhibiting succinic acid 1,3(S)-diamino-4-phenyl-2(R)-butanol derivs.)

IT 13335-71-2P, (2,6-Dimethylphenoxy)acetic acid 170359-24-7P 181038-41-5P 181038-45-9P 181038-49-3P 181038-52-8P 181229-34-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(HIV protease inhibiting succinic acid 1,3(S)-diamino-4-phenyl-2(R)-butanol derivs.)

IT 144114-21-6, Retropepsin
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(HIV protease-inhibiting succinic acid 1,3(S)-diamino-4-phenyl-2(R)-butanol derivs.)

L17 ANSWER 7 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 125:222432 MARPAT
TI Preparation of .alpha.-aminoboronic acid and ester as inhibitors of thrombin
IN Amparo, Eugene Cruz; Miller, William Henry; Pacofsky, Gregory James; Wityak, John; Weber, Patricia Carol; Duncia, John Jonas Vytautas; Santella, Joseph Basil, III
PA The Du Pont Merck Pharmaceutical Company, USA
SO PCT Int. Appl., 416 pp.
CODEN: PIXXD2
PI WO 9620689 A2 960711
DS W: AU, CA, JP, MX, NZ
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 95-US16248 951213
PRAI US 94-364338 941227
DT Patent
LA English
AB Novel boronic acid and ester and carboxyl-modified amino acid

compds. of formula R1-Z-CHR1-A [A = BY1Y2, CO CF3, CO2R3, COCO2R3, COCOR3, PO3H2, CHO, etc.; wherein Y1, Y2 = OH, F, NR3R4, C1-8 alkoxy; or Y1 and Y2 are taken together to form a cyclic boron ester, cyclic boron amide, or cyclic boron amide ester contg. 2-20 C atoms and 0-3 heteroatoms selected from N, S, or S; R3 = H, C1-8 alkyl, aryl-C1-4 alkyl, C5-7 cycloalkyl, Ph; R4 = group listed in R3, phenylsulfonyl; Z = (CH2)m CON R8, (CH2)m C(S)NR8, (CH2)m CO2, (CH2)m C(S)O, (CH2)mSO2O; wherein m = 0-6 and R8 = H, ring-(un)substituted phenylalkyl, C3-7 cycloalkyl, C1-8 alkyl; R1 = ring-substituted arylalkyl or heteroaryl, etc.; R2 = substituted C1-12 alkyl or C2-12 alkenyl, (substituted alkyl)phenylalkyl], which are inhibitors of trypsin-like enzymes, notably blood coagulation proteases such as human thrombin, factor VIIa, factor IXa, factor Xa, plasma kallikrein, and plasmin, and are useful for the treatment of thrombosis and inflammation or as anticoagulants for the processing of blood for therapeutic or diagnostic purposes or for the prodn. of blood products or fragments, are prepd. Thus, (+)-pinanediol 4-bromo-1(R)-aminobutane-1-boronate hydrochloride was acylated by 4-phenylbenzoyl chloride in the presence of N-methylmorpholine in CH2Cl2 to give (+)-pinanediol 4-bromo-1(R)-(4-phenylbenzoylamino)butane-1-boronate, which underwent azidolysis with NaN3 in DMF at 70.degree. for 2 h to give (+)-pinanediol 4-azido-1(R)-(4-phenylbenzoylamino)butane-1-boronate, and catalytic hydrogenation in the presence of Pd(OH)2/C in a mixt. of MeOH and 1 M aq. HCl to give (+)-pinanediol 4-amino-1(R)-(4-phenylbenzoylamino)butane-1-boronate, i.e., N1-(4-phenylbenzoyl)boroornithine (+)-pinanediol ester hydrochloride, followed by condensation with aminoiminomethanesulfonic acid in the presence of 4-dimethylaminopyridine in ethanol at reflux of 3 h to give N-(4-phenylbenzoyl)boroarginine (+)-pinanediol ester, bisulfite. The latter compd. in vitro inhibited human thrombin and factor Xa with Ki value of <500 and 50,000 nM, resp.

IC ICM A61K

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 29

ST antithrombotic antiinflammatory boronic acid ester; boronic acid ester prepn inhibitor thrombin; boroarginine pinanediol blood coagulation protease inhibitor

IT Anticoagulants and Antithrombotics
Inflammation inhibitors
(prepn. of .alpha.-aminoboronic acids and esters as inhibitors of blood coagulation proteases for disease therapy)

IT Amino acids, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(analogs, boron-contg.; prepn. of .alpha.-aminoboronic acids and esters as inhibitors of blood coagulation proteases for disease therapy)

IT 180897-32-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nod oh,dprepn. of .alpha.-aminoboronic acids and esters as inhibitors of blood coagulation proteases for disease therapy)

IT 180896-86-0P 180896-92-8P 180896-93-9P 180896-95-1P
180897-02-3P 180897-04-5P 180897-05-6P 180897-06-7P
180897-07-8P 180897-08-9P 180897-09-0P 180897-10-3P
180897-11-4P 180897-12-5P 180897-13-6P 180897-14-7P
180897-15-8P 180897-16-9P 180897-17-0P 180897-18-1P

180897-19-2P 180897-20-5P 180897-21-6P 180897-22-7P
180897-23-8P 180897-24-9P 180897-25-0P 180897-26-1P
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180897-48-7P 180897-49-8P 180897-50-1P 180897-51-2P
180897-52-3P 180897-53-4P 180897-54-5P 180897-55-6P
180897-56-7P 180897-57-8P 180897-58-9P 180897-59-0P
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180898-00-4P 180898-01-5P 180898-02-6P 180898-03-7P
180898-04-8P 180898-05-9P 180898-06-0P 180898-07-1P
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181138-69-2P 181138-70-5P 181138-71-6P 181138-72-7P
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181138-93-2P 181138-94-3P 181138-95-4P 181138-96-5P
181138-97-6P 181138-98-7P 181138-99-8P 181139-00-4P
181139-01-5P 181139-02-6P 181139-03-7P 181139-04-8P
181139-05-9P 181139-06-0P 181139-07-1P 181139-08-2P
181139-09-3P 181139-10-6P 181139-11-7P 181139-12-8P
181139-13-9P 181139-14-0P 181139-15-1P 181139-16-2P
181139-17-3P 181139-18-4P 181227-37-2P 181227-38-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .alpha.-aminoboronic acids and esters as inhibitors of blood coagulation proteases for disease therapy)

IT 9002-04-4, Thrombin 9002-05-5, Factor Xa 37259-58-8, Serine protease 65312-43-8, Blood-coagulation factor VIIa
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of .alpha.-aminoboronic acids and esters as inhibitors of blood coagulation proteases for disease therapy)

IT 62-56-6, Thiourea, reactions 76-83-5, Trityl chloride 105-36-2, Ethyl bromoacetate 140-29-4, Phenylacetonitrile 140-87-4, Cyanoacetylhydrazine 868-59-7 1184-90-3, Aminoiminomethanesulfonic acid 13226-93-2 14002-51-8, 4-Phenylbenzoyl chloride 26628-22-8, Sodium azide 131100-00-0 165881-38-9

Searcher : Shears 308-4994

RL: RCT (Reactant)
(prepn. of .alpha.-aminoboronic acids and esters as inhibitors of blood coagulation proteases for disease therapy)

IT 5333-86-8P 57723-86-1P 103249-79-2P 180896-85-9P
180896-87-1P 180896-88-2P 180896-89-3P 180896-90-6P
180896-91-7P 180896-94-0P 180896-96-2P 180896-99-5P
180897-01-2P 181033-28-3P 181033-29-4P 181033-30-7P
181138-47-6P 181138-48-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of .alpha.-aminoboronic acids and esters as inhibitors of blood coagulation proteases for disease therapy)

L17 ANSWER 8 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 125:185902 MARPAT
TI Use of a tachykinin antagonist and an opioid analgesic for a pharmaceutical analgesic combination, and tachykinin antagonist prepn.
IN Hill, Raymond George
PA Merck Sharp and Dohme Limited, UK
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
PI WO 9620009 A1 960704
DS W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-GB2931 951215
PRAI GB 94-26102 941223
DT Patent
LA English
AB A tachykinin antagonist and an opioid analgesic are used for manuf. of a medicament for the treatment or prevention of pain or nociception. Also provided are pharmaceutical compns. and products comprising a tachykinin antagonist and an opioid analgesic. Prepn. of e.g. 2-(R)-[1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy]-4-[5-(dimethylaminomethyl)-1,2,3-triazol-4-yl]methyl-3-(S)-(4-fluorophenyl)morpholine is described. Active-ingredient formulations are included.
IC ICM A61K045-06
CC 1-11 (Pharmacology)
Section cross-reference(s): 28, 63
ST tachykinin antagonist opioid analgesic combination antinociceptive; morpholine deriv prepn analgesic pharmaceutical combination
IT Analgesics
Drug interactions
Pharmaceutical dosage forms
Resolution
(tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)
IT Opioids
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)
IT Pharmaceutical dosage forms
(injections, tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT Pharmaceutical dosage forms
(injections, emulsions, tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT Pharmaceutical dosage forms
(parenterals, tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT Pharmaceutical dosage forms
(tablets, tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT Kinin receptors
Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(tachykinin, tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT Kinin receptors
Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(tachykinin NK1, tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT Pharmaceutical dosage forms
(topical, tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT 459-04-1P 1271-66-5P, Dimethyl titanocene 19883-57-9P, (S)-(4-Fluorophenyl)glycine 24843-91-2P 42718-13-8P 71783-54-5P 159706-87-3P 159707-16-1P 159707-17-2P 159707-18-3P 170729-77-8P 170902-74-6P 170902-75-7P 171243-11-1P 171243-12-2P 171243-13-3P 171243-14-4P 171243-15-5P 171338-27-5P 178616-85-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction; tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT 79-44-7, N,N-Dimethylcarbamoyl chloride 100-52-7, Benzaldehyde, reactions 106-93-4, 1,2-Dibromoethane 106-96-7, Propargyl bromide 405-50-5, 4-Fluorophenylacetic acid 785-56-8, 3,5-Bis(trifluoromethyl)benzoyl chloride 821-10-3 990-91-0, Tetrabenzyl pyrophosphate 1271-19-8, Titanocene dichloride 2743-38-6 3282-30-2, Trimethylacetyl chloride 7087-68-5, N,N-Diisopropylethylamine 17026-42-5 36982-84-0, 2,4,6-Triisopropylphenylsulfonyl azide 90719-32-7, 4-(S)-Benzyl-2-oxazolidinone
RL: RCT (Reactant)
(reaction; tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT 57-27-2, Morphine, biological studies 136982-36-0, CP-99,994 136982-37-1, CP-100,263
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT 171242-93-6P 171482-05-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT 170729-80-3P 171242-11-8P 171242-15-2P 171242-24-3P 180595-28-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

IT 57-42-1, Meperidine 76-41-5, Oxymorphone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 359-83-1, Pentazocine 437-38-7, Fentanyl 466-99-9, Hydromorphone 469-62-5, Propoxyphene 561-27-3, Diacetylmorphine 20594-83-6, Nalbuphine 42408-82-2, Butorphanol 52485-79-7, Buprenorphine 56030-54-7 71195-58-9, Alfentanil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tachykinin antagonist and opioid analgesic for pharmaceutical analgesic combination, and tachykinin antagonist prepn.)

L17 ANSWER 9 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 125:59145 MARPAT
TI N-Terminus modified peptide analogs of LHRH as LHRH antagonists
IN Haviv, Fortuna; Fitzpatrick, Timothy D.; Swenson, Rolf E.; Nichols, Charles J.; Mort, Nicholas A.
PA Tap Holdings Inc., USA
SO U.S., 33 pp. Cont.-in-part of U.S. Ser. No. 103,474, abandoned.
CODEN: USXXAM
PI US 5502035 A 960326
AI US 94-279677 940727
PRAI US 93-103474 930806
DT Patent
LA English
AB Decapaptide and undecapaptides substituted on the N-terminal nitrogen atom by acyl groups which include furo-2-yl, isonicotinyl, nicotinyl, 2-, 3-, and 4-quinolinecarbonyl, shikimyl, dihydroshikimyl, and tetrahydrofur-2-oyl are potent antagonists of LHRH and are useful for suppressing the levels of sex hormones in mammals. Thus, e.g., N-Ac-D-Tyr-D-2Nal-D-4ClPhe-D-3Pal-Ser-NMeTyr-D-Lys(N-.epsilon.-nicotinyl)-Leu-Lys(N-.epsilon.-isopropyl)-Pro-D-Ala-NH2 [D-2Nal = D-3-(naphth-2-yl)alanine, D-3Pal = D-3-(pyrid-3-yl)alanine] was prepd. in a peptide synthesizer and exhibited in vitro LHRH antagonist potency of pA2 = 10.75, where pA2 = neg. logarithm of the concn. of antagonist required to shift the response curve produced by the agonist leuprolide to two-fold higher concn.
IC ICM C07K014-59
NCL 514015000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2, 63
ST peptide LHRH antagonist sex hormone suppression
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(deca-, N-terminus modified peptide analogs of LHRH as LHRH antagonists)
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(undeca-, N-terminus modified peptide analogs of LHRH as LHRH antagonists)

IT 157147-52-9P 168192-25-4P 168192-26-5P 168192-27-6P
168192-28-7P 168192-29-8P 168192-30-1P 168192-31-2P
168192-34-5P 168192-35-6P 168192-36-7P 168192-38-9P
168192-39-0P 168192-40-3P 168192-41-4P 168192-42-5P
168192-43-6P 168192-80-1P 168192-92-5P 168192-94-7P
168192-95-8P 168192-96-9P 168192-97-0P 168192-98-1P
168192-99-2P 168193-00-8P 168193-01-9P 168193-02-0P
168193-03-1P 168193-04-2P 168193-05-3P 168193-06-4P
168193-07-5P 168193-08-6P 168193-09-7P 168193-10-0P
168193-11-1P 168193-12-2P 168193-13-3P 168193-15-5P
168193-16-6P 168193-17-7P 168193-18-8P 168193-19-9P
168193-21-3P 168193-22-4P 168193-23-5P 168193-24-6P
168193-25-7P 168193-26-8P 168193-27-9P 168193-28-0P
168193-29-1P 168193-30-4P 168193-31-5P 168193-32-6P
168193-34-8P 168193-35-9P 168193-53-1P 168193-54-2P
168193-55-3P 168193-56-4P 168193-57-5P 168193-58-6P
168193-59-7P 168193-60-0P 168193-67-7P 168193-71-3P
168193-87-1P 168394-99-8P 168395-00-4P 168395-21-9P
168395-22-0P 168395-24-2P 168395-25-3P 177614-72-1P
177614-73-2P 177614-74-3P 177614-75-4P 177614-76-5P
177614-77-6P 177614-78-7P 177614-79-8P 177614-80-1P
177614-81-2P 177614-82-3P 177614-83-4P 177614-84-5P
177614-85-6P 177614-86-7P 177614-87-8P 177614-88-9P
177614-89-0P 177614-91-4P 177614-92-5P 177614-93-6P
177614-94-7P 177614-95-8P 177614-96-9P 177614-97-0P
177767-47-4P 177767-48-5P 177767-49-6P 177767-51-0P
177767-52-1P 177767-53-2P 177767-54-3P 177767-55-4P
177767-56-5P 177767-57-6P 177767-58-7P 177767-59-8P
177767-60-1P 177767-61-2P 177767-62-3P 177767-63-4P
177767-64-5P 177767-65-6P 177767-66-7P 177767-67-8P
177767-68-9P 177767-69-0P 177767-70-3P 177767-71-4P
177767-72-5P 177767-73-6P 177767-74-7P 177767-75-8P
177767-76-9P 177767-77-0P 177767-78-1P 177767-79-2P
177767-80-5P 177767-81-6P 177767-82-7P 177767-83-8P
177767-84-9P 177767-85-0P 177767-86-1P 177767-87-2P
177767-88-3P 177767-89-4P 177767-90-7P 177767-91-8P
177767-92-9P 177767-93-0P 177767-94-1P 177767-95-2P
177767-96-3P 177767-97-4P 177767-98-5P 177768-00-2P
177768-01-3P 177768-02-4P 177768-03-5P 177768-04-6P
177768-05-7P 177768-06-8P 177768-07-9P 177768-08-0P
177768-09-1P 177768-10-4P 177768-11-5P 177768-12-6P
177768-13-7P 177768-15-9P 177768-16-0P 177768-17-1P
177768-18-2P 177768-19-3P 177768-20-6P 177768-21-7P
177768-22-8P 177768-23-9P 177768-24-0P 177929-80-5P
177929-81-6P 178033-65-3P 178033-66-4P 178033-67-5P
178033-68-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-terminus modified peptide analogs of LHRH as LHRH antagonists)

IT 9034-40-6, LHRH
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(N-terminus modified peptide analogs of LHRH as LHRH antagonists)

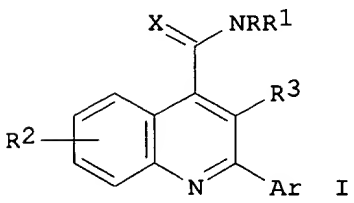
IT 59-67-6, Nicotinic acid, reactions 98-59-9, p-Toluenesulfonyl chloride 138-59-0, Shikimic acid 553-53-7, Nicotinyl hydrazide 2188-18-3 3303-84-2, Boc-3-aminopropanoic acid 3326-71-4 6404-29-1, Boc-6-aminocaproic acid 7764-95-6 7764-95-6D,

4-methylbenzhydrylamine resin bound 13139-15-6 13139-16-7
13734-36-6 13734-36-6D, amino-substituted resin bound 13836-37-8
14609-04-2 15761-38-3D, amino-substituted resin bound 15761-39-4
16874-33-2, Tetrahydro-2-furoic acid 16937-99-8 18942-49-9
21835-19-8 23680-31-1, Boc-O-benzylserine 37553-65-4,
Boc-N-methylphenylalanine 37784-17-1 47173-80-8,
Boc-D-O-benzylserine 51077-14-6 53363-89-6, Boc-N-methylleucine
54689-36-0, L-Gulonic lactone 56558-31-7 57292-44-1,
Boc-D-4-chlorophenylalanine 57294-38-9 58438-04-3,
Boc-(2-naphthyl)alanine 66838-42-4, (R)-Tetrahydro-3-furoic acid
68090-88-0, Boc-4-chlorophenylalanine 76932-48-4,
Boc-D-(naphth-1-yl)alanine 76985-10-9, Boc-D-(2-naphthyl)alanine
87392-05-0, (R)-Tetrahydro-2-furoic acid 87392-07-2,
(S)-Tetrahydro-2-furoic acid 98266-33-2 115186-31-7
117142-26-4, Boc-(3-pyridyl)alanine 121080-95-3, Boc-D-citrulline
121080-97-5, Boc-D-homocitrulline 122546-52-5 125323-99-1
135101-22-3 168193-97-3 168395-26-4, (S)-Tetrahydro-3-furoic
acid 177614-98-1 177614-99-2 177615-00-8 177615-02-0,
Boc-4-aminoheptanoic acid
RL: RCT (Reactant)
(N-terminus modified peptide analogs of LHRH as LHRH antagonists)

IT 177615-01-9DP, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(N-terminus modified peptide analogs of LHRH as LHRH antagonists)

IT 9002-67-9, LH
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(suppression; N-terminus modified peptide analogs of LHRH as LHRH antagonists)

L17 ANSWER 10 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 125:33490 MARPAT
TI Preparation of quinoline-4-carboxamides and related compounds as as NK3 antagonists.
IN Farina, Carlo; Giardina, Giuseppe Arnaldo Mari; Grugni, Mario; Raveglia, Luca Francesco
PA Smithkline Beecham Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
PI WO 9602509 A1 960201
DS W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 95-EP2638 950706
PRAI IT 94-MI1466 940714
DT Patent
LA English
GI



I

AB Title compds. [I; Ar = (substituted) Ph, naphthyl, heterocyclyl; R = (substituted) Ph, heterocyclyl, CHR4R5; R4 = H, alkyl, cycloalkyl, (substituted) Ph, heteroaryl, etc.; R5 = alkyl, (CH2)nAr; n = 0-3; R1 = H, alkyl; R2, R3 = H, alkyl, alkenyl, aryl, carboxamido, sulfonamido, alkoxy, OH, halo, NO2, cyano, hydroxyalkyl, aminoalkyl, acylamino, CO2H, alkylsulfonylamino, etc; X = O, S, H2, NCN], were prepd. Thus, benzylamine, 2-phenylquinoline-4-carbonyl chloride, and K2CO3 were stirred in DMF at 0.degree.-room temp. overnight to give N-benzyl-2-phenylquinoline-4-carboxamide. The latter inhibited binding of 125I-N-Me-Phe7-NKB to guinea pig cortical membranes with IC50 = 620 nM.

IC ICM C07D215-52
ICS A61K031-47; C07D215-20; C07D401-12

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinolinecarboxamide prepn neurokinin antagonist

IT Analgesics
Anticonvulsants and Antiepileptics
Antidepressants
Anxiolytics
(prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Eye
Hay fever
Psoriasis
(treatment of inflammation; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Kidney, disease
Parkinsonism
Skin, disease
(treatment; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Bronchodilators
(antiasthmatics, prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Tranquilizers and Neuroleptics
(antipsychotics, prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Dermatitis
(atopic, treatment; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Lung, disease
(chronic obstructive, treatment; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Nervous system
(disease, Huntington's chorea, treatment of inflammation; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Nervous system
(disease, degeneration, treatment of inflammation; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Bladder
(disease, incontinence, treatment; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT Appetite
(disorder, treatment of inflammation; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

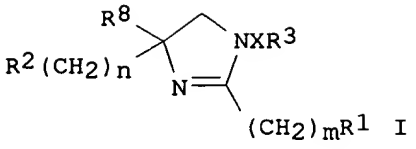
IT Kinins (animal hormones)
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(neuro-, antagonists; prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT 177360-16-6P 177360-17-7P 177360-18-8P 177360-19-9P
177360-20-2P 177360-21-3P 177360-22-4P 177360-23-5P
177360-24-6P 177360-25-7P 177360-26-8P 177360-27-9P
177360-28-0P 177606-27-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

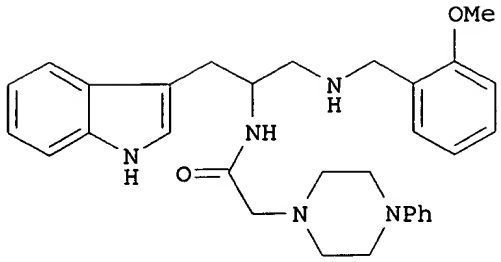
IT 62-53-3, Aniline, reactions 64-04-0, Phenethylamine 98-86-2, Acetophenone, reactions 100-46-9, Benzylamine, reactions 132-60-5, 2-Phenylquinoline-4-carboxylic acid 134-20-3, Methyl anthranilate 1226-34-2 3731-51-9, 2-Aminomethylpyridine 5763-61-1, 3,4-Dimethoxybenzylamine 6850-57-3, 2-Methoxybenzylamine 7524-50-7 21685-47-2, D-Valine methyl ester 43071-45-0, 3-Methyl-2-phenylquinoline-4-carboxylic acid 52351-75-4, 6-Methoxyisatin 85068-29-7, 3,5-Bis(trifluoromethyl)benzylamine
RL: RCT (Reactant)
(prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

IT 59661-86-8P 174636-63-6P 174636-64-7P 177360-29-1P
177360-30-4P 177360-31-5P 177360-32-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

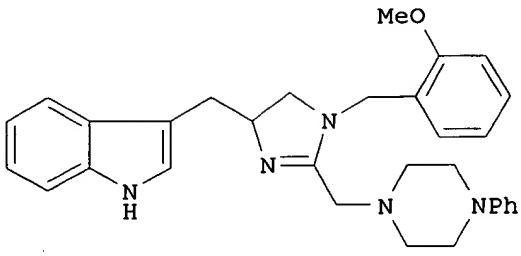
L17 ANSWER 11 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 124:343300 MARPAT
TI Preparation of imidazoline derivatives as tachykinin receptor antagonists
IN Hipskind, Philip Arthur; Howbert, James Jeffry; Muehl, Brian Stephen
PA Lilly, Eli, and Co., USA
SO Can. Pat. Appl., 61 pp.
CODEN: CPXXEB
PI CA 2151113 AA 951211
AI CA 95-2151113 950606
PRAI US 94-257966 940610
DT Patent
LA English
GI



I



II



III

AB The invention provides novel substituted 2-imidazolines I [X = (CHR4)p(CHR6)q; m, n, p, q = 0, 1; R1 = H, (un)substituted trityl, Ph, Ph2CH, PhO, PhS, piperazinyl, piperidinyl, indolyl, amino, leaving group, NHCH2R5, etc.; R2 = (un)substituted Ph, 2- or 3-indolyl or -indolinyl, benzothienyl, benzofuranyl, naphthyl; R3 = (un)substituted Ph, phenylalkylidene, cycloalkyl, alkyl, H, alkenyl, cycloalkenyl; R4, R6 = H, alkyl; R5 = pyridyl, anilinoalkylidenyl, anilinocarbonyl] and their salts and solvates. The compds. are useful in the treatment or prevention of a variety of physiol. disorders assocd. with an excess of tachykinins. For example, Boc-Trp-OH was converted in 4 steps to intermediate II, which was cyclized in 83% yield in refluxing 1,2-Cl2C6H4 to give title compd. III. In NK-1 and NK-2 receptor binding assays, III had IC50 values of 0.12 and 0.47 .mu.M, resp.

IC ICM C07D233-22
ICS C07D401-02; C07D403-00; C07D405-02; C07D409-02; C07D413-02; A61K031-395

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST imidazoline prepn tachykinin receptor antagonist

IT Allergy inhibitors
Analgesics
Antidepressants
Antiemetics
Anxiolytics
Immunosuppressants
Inflammation inhibitors
Nervous system agents
Nootropics
(prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Down's syndrome
Drug dependence
Eye, disease
Multiple sclerosis
Parkinsonism

Searcher : Shears 308-4994

Schizophrenia
Skin, disease
(treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Mental disorder
(Alzheimer's disease, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Intestine, disease
(Crohn's, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Blood vessel, disease
(Raynaud's phenomenon, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Heart, disease
(angina pectoris, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Bronchodilators
(antiasthmatics, prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Antiarteriosclerotics
(antiatherosclerotics, prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Tranquilizers and Neuroleptics
(antipsychotics, prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Lung, disease
(chronic obstructive, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Mental disorder
(dementia, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Digestive tract
(disease, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Nervous system
(disease, amyotrophic lateral sclerosis, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Prostate gland
(disease, benign hyperplasia, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Bladder
(disease, incontinence, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Intestine, disease
(irritable bowel syndrome, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Headache
(migraine, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Nerve, disease
(neuralgia, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Nerve, disease
(neuropathy, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Brain, disease
(stroke, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Kinin receptors
Receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(tachykinin, prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Kinin receptors
Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(tachykinin NK1, prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Kinin receptors
Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(tachykinin NK2, prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Kinins (animal hormones)
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinins, prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT Intestine, disease
(ulcerative colitis, treatment; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT 170567-70-1P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT 170568-24-8P
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation)
(byproduct; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

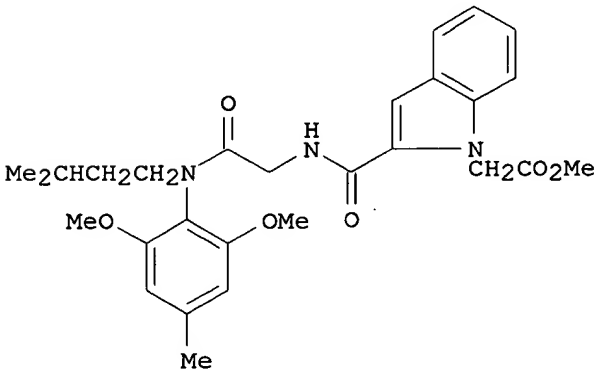
IT 3381-62-2P, .alpha.-(Tritylamino)phenylacetic acid 47672-25-3P, 3-Phenyl-2-(tritylamino)propanoic acid 170566-34-4P 170566-35-5P 170566-36-6P 170566-37-7P 170566-38-8P 170566-39-9P 170566-40-2P 170566-41-3P 170566-77-5P 170566-78-6P 170567-38-1P 170568-06-6P, 2-Phenyl-2-(tritylamino)-N-(2-methoxybenzyl)ethylamine 170568-07-7P, 1-Phenyl-2-(tritylamino)-3-[(2-methoxybenzyl)amino]propane 170568-08-8P 170568-10-2P 170568-11-3P 170568-12-4P 170568-13-5P 176249-62-0P, 2-Phenyl-2-(tritylamino)-N-(2-methoxybenzyl)acetamide 176249-63-1P 176249-64-2P 176249-65-3P 176249-66-4P 176249-67-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT 176249-58-4P 176249-59-5P 176249-60-8P 176249-61-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of imidazoline derivs. as tachykinin receptor antagonists)

IT 64-18-6, Formic acid, reactions 69-91-0, .alpha.-Aminophenylacetic acid 75-77-4, Trimethylsilyl chloride, reactions 76-83-5, Trityl chloride 108-24-7, Acetic anhydride 150-30-1, 3-Phenyl-2-aminopropanoic acid 830-03-5, p-Nitrophenyl acetate 6850-57-3, 2-Methoxybenzylamine 13139-14-5 13510-08-2, .alpha.-Methyltryptophan 170568-31-7, 2-(4-Phenylpiperazin-1-yl)acetic acid sodium salt
RL: RCT (Reactant)
(starting material; prepn. of imidazoline derivs. as tachykinin

receptor antagonists)

L17 ANSWER 12 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 124:343106 MARPAT
TI Preparation of N-aryl-N.alpha.-(indolylcarbonyl)glycineamides and analogs as cholecystokinin receptor agonists
IN Bras, Jean-Pierre; De Cointet, Paul; Despeyroux, Pierre; Frehel, Daniel; Gully, Danielle; Maffrand, Jean-Pierre; Bignon, Eric
PA Sanofi, Fr.
SO Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
PI EP 697403 A1 960221
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
AI EP 95-401912 950818
PRAI FR 94-10165 940819
DT Patent
LA French
GI



II

AB R1NRCOCHR2NHCOR3 [I; R = substituted 2-(MeO)C6H4, -2-methoxy-3-pyridyl, -4-methoxy-5-pyrimidinyl, naphthyl; R1 = (ar)alkyl, cycloalkyl(alkyl), alkoxyalkyl, (CH2)1-3COR4, etc.; R2 = H, (un)substituted alkyl; R3 = naphthyl, quinolyl, indolyl, etc.; R4 = pyrrolidino, piperidino, morpholino] were prepd. as CCK-A receptor agonists. Thus, Me2CHCH2CH2COCl was amidated by 2,6-dimethoxy-4-methylaniline and the reduced product amidated by Me3CO2CNHCH2CO2H to give, after deprotection, N-(2,6-dimethoxy-4-methylphenyl)-N-isopentylglycineamide which was amidated by N-(methoxycarbonylmethyl)indole-2-carboxylic acid to give title compd. II. Selected I had ED50 of 1mg/kg i.p. for blockage of gastric emptying in mice.
IC ICM C07D209-42
ICS A61K031-395; C07D405-04; C07D215-54; C07D215-48; C07D217-26; C07D487-06; C07C237-22
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
ST indolylcarbonylglycineamide prepn cholecystokinin receptor agonist
IT Nervous system agents
(prepn. of N-aryl-N.alpha.-(indolylcarbonyl)glycineamides and analogs as cholecystokinin receptor agonists)
IT Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL

(Biological study)
(cholecystokinin A, prepn. of N-aryl-N.alpha.-(indolylcarbonyl)glycineamides and analogs as cholecystokinin receptor agonists)

IT Digestive tract
(disease, treatment; prepn. of N-aryl-N.alpha.-(indolylcarbonyl)glycineamides and analogs as cholecystokinin receptor agonists)

IT 176526-27-5P 176526-28-6P 176526-29-7P 176526-30-0P
176526-31-1P 176526-32-2P 176526-33-3P 176526-34-4P
176526-35-5P 176526-36-6P 176526-37-7P 176526-38-8P
176526-39-9P 176526-40-2P 176526-41-3P 176526-42-4P
176526-43-5P 176526-44-6P 176526-45-7P 176526-46-8P
176526-47-9P 176526-48-0P 176526-49-1P 176526-50-4P
176526-51-5P 176526-52-6P 176526-53-7P 176526-54-8P
176526-55-9P 176526-56-0P 176526-57-1P 176526-58-2P
176526-59-3P 176526-60-6P 176526-61-7P 176526-62-8P
176526-63-9P 176526-64-0P 176526-65-1P 176526-66-2P
176526-67-3P 176526-68-4P 176526-69-5P 176526-70-8P
176526-71-9P 176526-72-0P 176526-73-1P 176526-74-2P
176526-75-3P 176526-76-4P 176526-77-5P 176526-78-6P
176526-79-7P 176526-80-0P 176526-81-1P 176526-82-2P
176526-83-3P 176526-84-4P 176526-85-5P 176526-86-6P
176526-87-7P 176526-88-8P 176526-89-9P 176526-90-2P
176526-91-3P 176526-92-4P 176526-93-5P 176526-94-6P
176526-95-7P 176526-96-8P 176526-97-9P 176526-98-0P
176526-99-1P 176527-00-7P 176527-01-8P 176527-02-9P
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176527-11-0P 176527-12-1P 176527-13-2P 176527-14-3P
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176527-19-8P 176527-20-1P 176527-21-2P 176527-22-3P
176527-23-4P 176527-24-5P 176527-25-6P 176527-26-7P
176527-27-8P 176527-28-9P 176527-29-0P 176527-30-3P
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176527-79-0P 176527-80-3P 176527-81-4P 176527-82-5P
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176527-87-0P 176527-88-1P 176527-89-2P 176527-90-5P
176527-91-6P 176527-92-7P 176527-93-8P 176527-94-9P
176527-95-0P 176527-96-1P 176527-97-2P 176527-98-3P
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176528-03-3P 176528-04-4P 176528-05-5P 176528-06-6P
176528-07-7P 176528-08-8P 176528-09-9P 176528-10-2P
176528-11-3P 176528-12-4P 176528-13-5P 176528-14-6P
176528-15-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-aryl-N.alpha.-(indolylcarbonyl)glycineamides and

analogs as cholecystokinin receptor agonists)

IT 108-12-3, Isovaleryl chloride 108-94-1, Cyclohexanone, reactions 621-82-9, Cinnamic acid, reactions 700-58-3, 2-Adamantanone 1477-50-5, 1H-Indole-2-carboxylic acid 4179-19-5, 3,5-Dimethoxytoluene 5452-37-9, Cyclooctylamine 13074-39-0, 2-Adamantanamine 30925-18-9, N-(tert-Butoxycarbonyl)aspartic acid benzyl ester 54812-41-8, 2,6-Dimethoxy-4-methylaniline 136382-26-8, N-(Methoxycarbonylmethyl)indole-2-carboxylic acid 176526-26-4
RL: RCT (Reactant)
(prepn. of N-aryl-N.alpha.-(indolylcarbonyl)glycineamides and analogs as cholecystokinin receptor agonists)

IT 56066-07-0P 83777-95-1P 121387-29-9P 176528-16-8P
176528-17-9P 176528-18-0P 176528-19-1P 176528-20-4P
176528-21-5P 176528-22-6P 176528-23-7P 176528-24-8P
176528-25-9P 176528-26-0P 176528-27-1P 176528-28-2P
176528-29-3P 176528-30-6P 176528-31-7P 176528-32-8P
176528-33-9P 176528-34-0P 176528-35-1P 176528-36-2P
176528-37-3P 176528-38-4P 176528-39-5P 176528-40-8P
176528-41-9P 176528-42-0P 176528-43-1P 176528-44-2P
176528-45-3P 176528-46-4P 176528-47-5P 176528-48-6P
176528-49-7P 176528-50-0P 176528-51-1P 176528-52-2P
176528-53-3P 176528-54-4P 176528-55-5P 176528-56-6P
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176528-61-3P 176528-62-4P 176528-63-5P 176528-64-6P
176528-65-7P 176528-66-8P 176528-67-9P 176528-68-0P
176528-69-1P 176528-70-4P 176528-71-5P 176528-72-6P
176528-73-7P 176528-74-8P 176528-75-9P 176528-76-0P
176528-77-1P 176528-78-2P 176528-79-3P 176528-80-6P
176528-81-7P 176528-82-8P 176528-83-9P 176528-84-0P
176528-85-1P 176528-86-2P 176528-87-3P 176528-88-4P
176528-89-5P 176528-90-8P 176528-91-9P 176528-92-0P
176528-93-1P 176528-94-2P 176528-95-3P 176528-96-4P
176528-97-5P 176528-98-6P 176528-99-7P 176529-00-3P
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176529-37-6P 176529-38-7P 176529-39-8P 176529-40-1P
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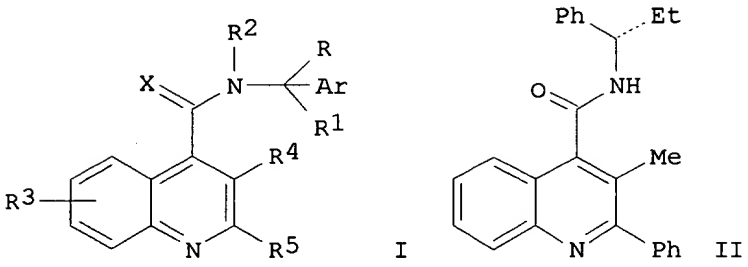
176529-45-6P 176529-46-7P 176529-47-8P 176529-48-9P
176529-49-0P 176529-50-3P 176529-51-4P 176529-52-5P
176529-53-6P 176529-54-7P 176529-55-8P 176529-56-9P
176529-57-0P 176529-58-1P 176529-59-2P 176529-60-5P
176529-61-6P 176529-62-7P 176529-63-8P 176529-64-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-aryl-N.alpha.-(indolylcarbonyl)glycineamides and analogs as cholecystokinin receptor agonists)

L17 ANSWER 13 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 124:232269 MARPAT
TI Quinoline derivatives as tachykinin NK3 receptor antagonists
IN Farina, Carlo; Giardina, Giuseppe Arnaldo Mari; Grugni, Mario; Raveglia, Luca Francesco
PA Smithkline Beecham Farmaceutici S.P.A., Italy

SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
PI WO 9532948 A1 951207
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-EP2000 950523
PRAI IT 94-MI1099 940527
IT 95-MI494 950314
DT Patent
LA English
GI



AB NK3 receptor antagonists I [Ar = (un)substituted Ph, naphthyl, cycloalkadienyl, heteroaryl; R = (un)substituted alkyl, cycloalkyl, (un)substituted Ph, phenylalkyl, or heteroaryl, CO2H and derivs., etc.; R1, R2 = H, alkyl; or R1R2 = (CH2)3-5; or RR1 = (CH2)2-5; R3, R4 = H, alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, amino, etc.; R5 = alkyl, cycloalkyl, (un)substituted (hetero)aryl; X = O, S, N(CN)] are useful in treating pulmonary, CNS, and neurodegenerative disorders, etc. Approx. 115 compds. were prepd. For example, amidation of 3-methyl-2-phenylquinoline-4-carbonyl chloride with (R)-.alpha.-ethylbenzylamine gave title compd. II in 58% yield. II had IC50 of 5.6 nM for displacement of [3H]-senktide from guinea-pig cortical NK3 receptors. Antagonist activity of I was shown by inhibition of senktide-induced contraction of guinea-pig ileum.

IC ICM C07D215-52
ICS A61K031-47; C07D409-04; C07D405-04; C07D401-04; C07D409-12; C07D221-18; C07D417-04; C07D401-12; C07D405-12
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
ST quinolinecarboxamide prepn tachykinin NK3 receptor antagonist
IT Allergy inhibitors
Analgesics
Anticonvulsants and Antiepileptics
Antidepressants
Anxiolytics
Inflammation inhibitors
Nervous system agents
(prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)
IT Antitussives

Hay fever
Kidney, disease
Parkinsonism
Psoriasis
Skin, disease
(treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Mental disorder
(Alzheimer's disease, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Bronchodilators
(antiasthmatics, prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Tranquilizers and Neuroleptics
(antipsychotics, prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Lung, disease
(chronic obstructive, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Nervous system
(disease, Huntington's chorea, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Nervous system
(disease, degeneration, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Bladder
(disease, incontinence, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Appetite
(disorder, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Behavior
(disorder, locomotor, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Eye, disease
(inflammation, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Inflammation
(neurogenic, treatment; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Kinin receptors
Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinin NK3, prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Kinins (animal hormones)
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinins, prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT 20146-25-2P, 2-(2-Furyl)quinoline-4-carboxylic acid 31792-47-9P, 2-(2-Thienyl)quinoline-4-carboxylic acid 59661-86-8P, 2-Phenylquinoline-4-carboxylic acid chloride 174636-63-6P, 7-Methoxy-2-phenylquinoline-4-carboxylic acid 174636-64-7P, 7-Methoxy-2-phenylquinoline-4-carboxylic acid chloride 174636-65-8P, 7-Hydroxy-2-phenylquinoline-4-carboxylic acid hydroiodide 174636-66-9P, 2-(2-Furyl)quinoline-4-carboxylic acid chloride 174636-67-0P, 2-(4-Pyridyl)quinoline-4-carboxylic acid

hydrochloride 174636-68-1P, 2-(4-Pyridyl)quinoline-4-carboxylic acid chloride hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT 174635-48-4P 174635-49-5P 174635-50-8P 174635-51-9P
174635-52-0P 174635-53-1P 174635-54-2P 174635-55-3P
174635-56-4P 174635-57-5P 174635-58-6P 174635-59-7P
174635-60-0P 174635-61-1P 174635-62-2P 174635-63-3P
174635-64-4P 174635-65-5P 174635-66-6P 174635-67-7P
174635-68-8P 174635-69-9P 174635-70-2P 174635-71-3P
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174635-76-8P 174635-77-9P 174635-78-0P 174635-79-1P
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174635-96-2P 174635-97-3P 174635-98-4P 174635-99-5P
174636-00-1P 174636-01-2P 174636-02-3P 174636-03-4P
174636-04-5P 174636-05-6P 174636-06-7P 174636-07-8P
174636-08-9P 174636-09-0P 174636-10-3P 174636-11-4P
174636-12-5P 174636-13-6P 174636-14-7P 174636-15-8P
174636-16-9P 174636-17-0P 174636-18-1P 174636-19-2P
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174636-24-9P 174636-25-0P 174636-26-1P 174636-27-2P
174636-28-3P 174636-29-4P 174636-30-7P 174636-31-8P
174636-32-9P 174636-33-0P 174636-34-1P 174636-35-2P
174636-36-3P 174636-37-4P 174636-38-5P 174636-39-6P
174636-40-9P 174636-41-0P 174636-42-1P 174636-43-2P
174636-44-3P 174636-45-4P 174636-46-5P 174636-47-6P
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174636-56-7P 174636-57-8P 174636-58-9P 174636-59-0P
174636-60-3P 174636-61-4P 174636-62-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT 83-93-2 88-15-3, 2-Acetylthiophene 91-00-9, (Diphenylmethyl)amine 91-56-5, Isatin 98-84-0, (R,S)-.alpha.-Methylbenzylamine 98-86-2, Acetophenone, reactions 124-40-3, reactions 132-60-5, 2-Phenylquinoline-4-carboxylic acid 485-89-2 541-88-8, Chloroacetic anhydride 574-98-1, 2-Phthalimidoethyl bromide 585-32-0, .alpha.,.alpha.-Dimethylbenzylamine 1032-45-7, 8-Hydroxy-2-phenylquinoline-4-carboxylic acid 1122-54-9, 4-Acetylpyridine 1192-62-7, 2-Acetylfuran 2627-86-3, (S)-(-)-.alpha.-Methylbenzylamine 2941-19-7, .alpha.-(n-Propyl)benzylamine 2941-20-0, .alpha.-Ethylbenzylamine 3082-64-2, (R)-.alpha.-Ethylbenzylamine 3789-59-1, (S)-.alpha.-Ethylbenzylamine 3886-69-9 4364-02-7, 2-(4-Methoxyphenyl)quinoline-4-carboxylic acid 4584-46-7, 2-(Dimethylamino)ethyl chloride hydrochloride 5050-41-9, 2-Pyrrolidinoethyl chloride 5407-04-5 5466-31-9, 2-(p-Chlorophenyl)quinoline-4-carboxylic acid 6633-62-1, 6-Chloro-2-phenylquinoline-4-carboxylic acid 6668-27-5, .alpha.-Isopropylbenzylamine 6952-34-7, 2-(4-Hydroxyphenyl)quinoline-4-carboxylic acid 7568-92-5, .alpha.-(Hydroxymethyl)benzylamine 13226-98-7, (D,L)-Methyl phenylglycinate hydrochloride 15028-39-4, (L)-Methyl

phenylglycinate hydrochloride 17380-74-4, 1-Phenylcyclopentylamine
19883-41-1, (D)-Methyl phenylglycinate hydrochloride 20389-05-3,
2-(4-Methylphenyl)quinoline-4-carboxylic acid 20389-09-7,
2-(2-Chlorophenyl)quinoline-4-carboxylic acid 20389-10-0,
2-(3-Chlorophenyl)quinoline-4-carboxylic acid 21908-20-3,
2-(2-Pyrrolyl)quinoline-4-carboxylic acid 24461-61-8, (R)-Methyl
phenylglycinate 25611-78-3, 1-Amino-1,2-diphenylethane
26682-99-5, Methyl phenylglycinate 30081-52-8,
2,3-Diphenylquinoline-4-carbonyl chloride 34698-41-4, 1-Aminoindan
36710-50-6, 3-Amino-5-methyl-2-phenylquinoline-4-carboxylic acid
36735-26-9, 3-Amino-2-phenylquinoline-4-carboxylic acid
37763-23-8, (R)-Methyl (4-hydroxyphenyl)glycinate 40023-89-0,
(.alpha.-Ethyl-3,4-dichlorobenzyl)amine 43071-45-0,
3-Methyl-2-phenylquinoline-4-carboxylic acid 51586-24-4,
.alpha.-(Trifluoromethyl)benzylamine 52351-75-4, 6-Methoxyisatin
52500-61-5, 1-Phenyl-2-hydroxypropylamine 57464-25-2,
3-Bromo-2-phenylquinoline-4-carboxylic acid 60289-68-1,
1-(4-Pyridyl)-n-propylamine 61501-03-9, .alpha.-n-Butylbenzylamine
74788-15-1, .alpha.-n-Heptylbenzylamine 74788-46-8 88831-43-0,
(R,S)-Methyl 3-amino-3-phenylpropionate hydrochloride 92566-43-3,
2-(2-Thiazolyl)quinoline-4-carboxylic acid 96669-82-8,
3-Phthalimido-2-phenylquinoline-4-carbonyl chloride 104236-44-4
107635-11-0, Methyl N-methylphenylglycinate 113131-95-6
132289-66-8, (D,L)-Methyl (2-thienyl)glycinate hydrochloride
148887-61-0, 2-(3,4-Dichlorophenyl)quinoline-4-carboxylic acid
174636-69-2, 3-Butyl-2-phenylquinoline-4-carbonyl chloride
174636-70-5, 3-Hexyl-2-phenylquinoline-4-carbonyl chloride
174636-71-6, 3-Methyl-2-phenylquinoline-4-carbonyl chloride
174636-72-7, 2-(2-Methoxyphenyl)quinoline-4-carbonyl chloride
174636-73-8, 2-(2-Fluorophenyl)quinoline-4-carbonyl chloride
174636-74-9, 7-Chloro-2-phenylquinoline-4-carbonyl chloride
174636-75-0, 6-Methyl-2-phenylquinoline-4-carbonyl chloride
174636-76-1, .alpha.-(Methoxymethyl)benzylamine 174636-77-2,
6-Chloro-2-phenylquinoline-4-carbonyl chloride 174636-78-3,
3-Ethyl-2-phenylquinoline-4-carbonyl chloride 174636-79-4,
3-n-Propyl-2-phenylquinoline-4-carbonyl chloride 174636-80-7,
6-Bromo-3-methyl-2-(4-bromophenyl)quinoline-4-carbonyl chloride
174636-81-8, 6-Bromo-3-methyl-2-phenylquinoline-4-carbonyl chloride
174636-82-9, 6-Methoxy-2-phenylquinoline-4-carbonyl chloride
174636-83-0, 2-(2-Benzofuryl)quinoline-4-carbonyl chloride
174636-84-1, 2-(3-Thienyl)quinoline-4-carboxylic acid 174636-85-2,
2-(2-Methylphenyl)quinoline-4-carboxylic acid 174636-86-3,
2-(3,4-Methylenedioxyphenyl)quinoline-4-carboxylic acid
174636-87-4, (.alpha.-Ethyl-p-methylbenzyl)amine 174636-88-5,
2-(3-Pyrrolyl)quinoline-4-carboxylic acid 174636-89-6,
(R)-.alpha.-(Phthalimidomethyl)benzylamine 174636-90-9,
3-Chloro-2-phenylquinoline-4-carboxylic acid 174636-91-0,
2-Cyclohexylquinoline-4-carboxylic acid 174636-92-1,
8-Acetoxy-2-phenylquinoline-4-carboxylic acid 174636-93-2,
2-(2,4-Dichlorophenyl)quinoline-4-carboxylic acid 174636-94-3
174636-95-4, 3-Methoxy-2-phenylquinoline-4-carboxylic acid chloride
174636-96-5, 5-Methyl-2-phenylquinoline-4-carboxylic acid
174636-97-6, 1-(2-Thienyl)-n-propylamine hydrochloride
174636-98-7, 3-Methyl-7-methoxy-2-phenylquinoline-4-carbonyl
chloride 174636-99-8, 3-Methoxy-5-methyl-2-phenylquinoline-4-
carboxylic acid
RL: RCT (Reactant)
(starting material; prepn. of quinolinecarboxamide derivs. as
tachykinin NK3 receptor antagonists)

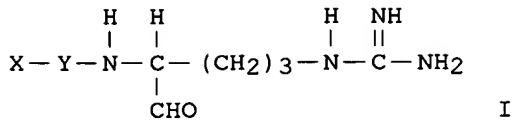
L17 ANSWER 14 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 124:87809 MARPAT
TI Preparation of peptidylargininealdehyde derivatives as antithrombotic agents.
IN Schacht, Aaron Leigh; Shuman, Robert Theodore; Smith, Gerald Floyd; Wikel, James Howard; Wiley, Michael Robert
PA Lilly, Eli, and Co., USA
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
PI WO 9523809 A1 950908
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-US2627 950303
PRAI US 94-206500 940304
US 94-318600 941005
DT Patent
LA English
AB YCOXNHCH(COR1)(CH2)3NHC(:NH)NH2 [R1 = H; X = Pro, azetidin-2-carbonyl; Y = R2ZNHCHR; R = PhCH2, Ph, cyclopentyl, cyclohexyl, cyclopentylmethyl, cyclohexylmethyl; Z = CO, SO, SO2; R2 = alkyl, perfluoroalkyl, alkoxy, alkoxyalkyl, cyclopentyl, cyclohexyl, amino, (substituted) aryl, etc.], were prepd. Thus, N-(1-methylindolyl-2-carbonyl)-D-phenylalanylprolylargininealdehyde hydrochloride (soln. phase prepn. given) showed a thrombin time (TT) of 43.
IC ICM C07K005-00
ICS C07K007-00; C07K017-00; A61K038-00; C07D417-00; C07D279-10; C07D279-12; C07D295-00; C07D413-00; C07D237-00; C07D237-02; C07D239-00; C07D239-02; C07D207-00; C07D205-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST peptidylargininealdehyde prepn antithrombotic; argininealdehyde peptidyl prepn antithrombotic
IT Anticoagulants and Antithrombotics
(prepn. of peptidylargininealdehyde derivs. as antithrombotic agents)
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptidylargininealdehyde derivs. as antithrombotic agents)
IT 9002-04-4, Thrombin
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(inhibitors; prepn. of peptidylargininealdehyde derivs. as antithrombotic agents)
IT 171180-52-2P 171180-53-3P 171180-54-4P 171180-58-8P
171180-59-9P 171180-60-2P 171180-61-3P 171180-62-4P
171180-63-5P 171180-64-6P 171180-65-7P 171180-66-8P
171180-67-9P 171180-69-1P 171180-70-4P 171180-71-5P
171180-72-6P 171180-73-7P 171180-74-8P 171180-75-9P
171180-76-0P 171180-77-1P 171180-78-2P 171180-79-3P
171180-80-6P 171180-81-7P 171180-82-8P 171180-83-9P
171180-84-0P 171335-93-6P 172412-71-4P 172412-72-5P
172584-70-2P 172584-71-3P 172584-72-4P 172584-73-5P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptidylargininealdehyde derivs. as antithrombotic agents)

IT 57-66-9 59-67-6, 3-Pyridinecarboxylic acid, reactions 75-36-5, Acetyl chloride 93-10-7, 2-Quinolinecarboxylic acid 98-09-9, Phenylsulfonyl chloride 98-66-8, p-Chlorophenylsulfonic acid 103-80-0, Phenylacetyl chloride 109-90-0, Ethyl isocyanate 124-63-0, Methanesulfonyl chloride 288-47-1, Thiazole 407-25-0, Trifluoroacetic anhydride 501-81-5, 3-Pyridylacetic acid 541-41-3, Ethyl chloroformate 594-44-5, Ethanesulfonyl chloride 1483-28-9, 2,5-Dimethoxyphenylsulfonyl chloride 2043-61-0, Cyclohexanecarboxaldehyde 2386-60-9, Butanesulfonyl chloride 2448-45-5 2719-27-9, Cyclohexanecarbonyl chloride 5292-43-3, tert-Butyl bromoacetate 5497-76-7 10147-36-1, Propanesulfonyl chloride 10147-37-2, Isopropylsulfonyl chloride 13360-57-1, Dimethylaminosulfonyl chloride 13918-92-8, 2,4-Difluorophenylsulfonyl chloride 16136-58-6, N-Methylindole-2-carboxylic acid 16652-71-4 18704-37-5, 8-Quinolylsulfonyl chloride 18942-49-9 33125-05-2, BOC-D-Phg-OH 35897-34-8 38870-89-2, MethoxyAcetyl chloride 57224-94-9 61367-40-6 69812-46-0 80466-79-1, 3,5-Dimethyl-4-isoxazolylsulfonyl chloride 127095-92-5, BOC-D-Cha-OH 149217-86-7
RL: RCT (Reactant)
(prepn. of peptidylargininealdehyde derivs. as antithrombotic agents)

IT 98-60-2P, p-Chlorophenylsulfonyl chloride 14328-64-4P 51219-18-2P 51219-20-6P 64471-88-1P, BOC-D-Phe-Pro-OBzl 96935-61-4P 100481-09-2P, Thiazole-2-sulfonyl chloride 138774-74-0P 144206-50-8P 171181-81-0P, H-D-Phe-Pro-OBzl.TFA 171181-82-1P 171181-83-2P 171181-84-3P 171181-85-4P 171181-86-5P 171181-87-6P 171181-88-7P 171181-90-1P 171181-93-4P 171181-94-5P 171181-95-6P 171181-96-7P 171181-97-8P 171181-98-9P 171336-09-7P 172348-96-8P 172348-97-9P 172412-73-6P 172412-74-7P 172412-75-8P 172412-76-9P, 2-Thiazolesulfonic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of peptidylargininealdehyde derivs. as antithrombotic agents)

L17 ANSWER 15 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 124:87806 MARPAT
TI L-Arginine aldehyde peptide derivatives useful as antithrombotic agents.
IN Schacht, Aaron Leigh; Smith, Gerald Floyd; Wiley, Michael Robert
PA Lilly, Eli, and Co., USA
SO Eur. Pat. Appl., 51 pp.
CODEN: EPXXDW
PI EP 672659 A1 950920
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
AI EP 95-301390 950303
PRAI US 94-206351 940304
DT Patent
LA English
GI



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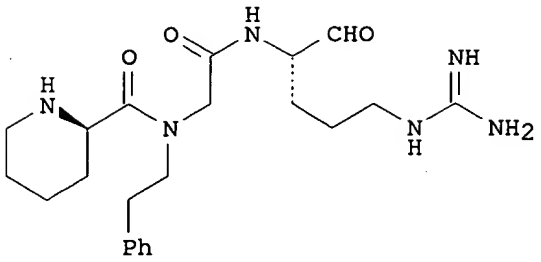


II

AB The invention relates to L-arginine aldehyde derivs. I [X = prolinyl, homoprolinyl, T(CH2)aC(R')(Q)CO, etc.; T = cycloalkyl, alkyl, (un)substituted Ph or naphthyl; a = 0, 1; R' = H, alkyl; Q = OH, alkoxy, (un)substituted NH2; Y = NRCH2CO; R = cycloalkyl, optionally heteroatom-interrupted and/or substituted alkyl] and their pharmaceutically acceptable salts and/or solvates. The compds. are useful as thrombin inhibitors, coagulation inhibitors, and thromboembolic disorder agents. For example, a sequence involving N-alkylation of PhCH2CH2NH2 with BrCH2CO2Bu-tert (56%), peptide coupling with Cbz-D-hPro-OH [Cbz = carbobenzyloxy, hPro = homoproline] (56%), C-terminal deprotection (100%), peptide coupling with H-Arg(Cbz)-lactam.2HCl (53%), and redn. with LiAlH4 at -78.degree. followed by hydrogenative deprotection (53%), gave title compd. II.2HCl, a preferred compd. In a human plasma anticoagulation assay, the above compd. doubled clotting time at 64 ng/mL. It also showed an oral/i.v. activity ratio of 17% in rats. Prepns. of 19 I and their intermediates, 8 formulations, and biol. results for I are given. In vitro enzyme inhibition tests showed high selectivity for thrombin over factor Xa, trypsin, plasmin, and t-PA.

IC ICM C07D211-60
ICS A61K031-445; C07C311-03; C07C279-12; C07D207-16
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST arginine aldehyde peptide prepn antithrombotic anticoagulant; thrombin inhibitor arginine aldehyde peptide prepn
IT Anticoagulants and Antithrombotics
Drug bioavailability
(prepn. of arginine aldehyde peptide derivs. as antithrombotics)
IT Aldehydes, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide, prepn. of arginine aldehyde peptide derivs. as antithrombotics)
IT 28697-09-8P, Cbz-D-hPro-OH 51219-18-2P 51219-20-6P
66116-14-1P, Pr-Gly-OBu-tert 66116-15-2P, Isobutyl-Gly-OBu-tert
66937-52-8P 127983-07-7P, Isopropyl-Gly-OBu-tert 144206-50-8P
158679-68-6P 158679-90-4P 165197-45-5P 172316-64-2P
172316-65-3P 172316-66-4P 172316-67-5P 172316-68-6P
172316-69-7P 172316-70-0P 172316-71-1P 172316-72-2P

172316-73-3P 172316-74-4P 172316-75-5P 172316-76-6P
172316-77-7P 172316-78-8P 172316-79-9P 172316-80-2P
172316-81-3P 172316-82-4P 172316-83-5P 172316-84-6P
172316-85-7P 172316-86-8P 172316-87-9P 172316-88-0P
172316-89-1P 172316-90-4P 172316-91-5P 172316-92-6P
172316-93-7P 172316-94-8P 172316-95-9P 172316-96-0P
172316-97-1P 172316-98-2P 172316-99-3P 172317-00-9P
172317-01-0P 172317-02-1P 172317-03-2P 172317-04-3P
172317-05-4P 172317-06-5P 172317-07-6P 172317-08-7P
172317-09-8P 172317-10-1P 172317-11-2P 172317-12-3P
172317-13-4P 172317-14-5P 172317-15-6P 172317-16-7P
172317-17-8P, Et-Gly-OBu-tert 172317-18-9P 172317-19-0P,
EtSO2-D-Phe-OH
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of arginine aldehyde peptide derivs. as antithrombotics)

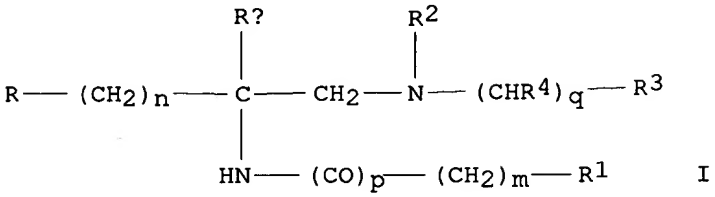
IT 172316-46-0P 172316-47-1P 172316-48-2P 172316-49-3P
172316-50-6P 172316-51-7P 172316-52-8P 172316-53-9P
172316-54-0P 172316-55-1P 172316-56-2P 172316-57-3P
172316-58-4P 172316-59-5P 172316-60-8P 172316-61-9P
172316-62-0P 172316-63-1P 172487-12-6P 172487-13-7P
172487-14-8P 172487-15-9P 172487-16-0P 172487-17-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arginine aldehyde peptide derivs. as antithrombotics)

IT 9001-90-5, Plasmin 9002-04-4, Thrombin 9002-05-5, Factor Xa
9002-07-7, Trypsin 139639-23-9, Tissue plasminogen activator
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of arginine aldehyde peptide derivs. as antithrombotics)

IT 62-53-3, Benzenamine, reactions 64-04-0, Phenethylamine 75-04-7, Ethylamine, reactions 75-31-0, Isopropylamine, reactions
78-81-9, Isobutylamine 95-53-4, o-Methylaniline, reactions
104-53-0, 3-Phenylpropionaldehyde 105-36-2, Ethyl bromoacetate
107-10-8, n-Propylamine, reactions 107-85-7, Isoamylamine
501-53-1, Benzyl chloroformate 594-44-5, Ethanesulfonyl chloride
673-06-3, H-D-Phe-OH 1148-11-4, Cbz-L-Pro-OH 1723-00-8,
H-D-HPro-OH 2495-35-4, Benzyl acrylate 5292-43-3, tert-Butyl bromoacetate 5664-21-1, Cyclohexylacetaldehyde 5680-79-5,
Glycine methyl ester hydrochloride 6404-31-5, Cbz-D-Pro-OH
6436-90-4, Bn-Gly-OEt 6937-16-2, Ethyl 4-aminobutyrate hydrochloride 13200-60-7, Me-Gly-OEt 14660-52-7, Ethyl 5-bromovalerate 27532-96-3, Glycine tert-butyl ester hydrochloride
35897-34-8 39608-31-6, Cbz-Sar-OH 52605-49-9, Sarcosine ethyl ester hydrochloride
RL: RCT (Reactant)
(starting material; prepn. of arginine aldehyde peptide derivs. as antithrombotics)

L17 ANSWER 16 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 123:339728 MARPAT
TI Non-peptide tachykinin receptor antagonists
IN Cho, Sung-Yong Stephen; Crowell, Thomas Alan; Gitter, Bruce Donald; Hipskind, Philip Arthur; Howbert, James Jeffry; Krushinski, Joseph Herman, Jr.; Lobb, Karen Lynn; Muehl, Brian Stephen; Nixon, James Arthur
PA Lilly, Eli, and Co., USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2

PI WO 9514017 A1 950526
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 94-US13222 941116
PRAI US 93-153847 931117
DT Patent
LA English
OS CASREACT 123:339728
GI



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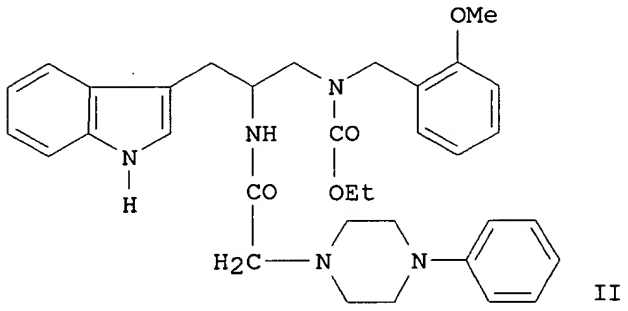

II

AB The invention provides a novel series of non-peptide compds. I [m, n, p = 0, 1; q = 0, 1, 2; R = (un)substituted Ph, 2- or 3-indolyl or -indolinyl, benzothienyl, benzofuranyl, or naphthyl; R1 = (un)substituted trityl, Ph, PhO, PhS, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, indolyl, amino, H, leaving group, etc.; R2 = H, alkyl, arylsulfonyl, alkylsulfonyl, carboxyalkyl, alkoxycarbonylalkyl, acyl; R3 = H, (un)substituted Ph, phenylalkyl, (cyclo)alk(en)yl, naphthyl; R4 = H, alkyl; R3 .noteq. H or alk(en)yl if R1 = H or halo] and their salts and solvates. The compds. are useful in the treatment or prevention of physiol. disorders assocd. with excess tachykinins. This invention also provides methods of treatment and pharmaceutical formulations employing I. Over 170 examples were prepd. and tested for biol. activity, and 11 formulations are described. For instance, activation of N-(tert-butoxycarbonyl)tryptophan with carbonyldiimidazole (CDI) and reaction with 2-MeOC6H4CH2NH2 gave 80.8% of the corresponding 2-methoxybenzylamide, which was deprotected (94.2%), reduced at the amide carbonyl with BH3.SMe2, coupled with Na 2-(4-phenylpiperazin-1-yl)acetic acid using CDI, and N-acylated with ClCO2Et and Et3N, to give title compd. II. This compd. had IC50 values of 1.7 and 1000 nM for binding to human NK-1 and NK-2 receptors, resp., in cultured cell assays.

Searcher : Shears 308-4994

IC ICM C07D403-12
ICS C07D401-12; C07D401-14; C07D413-12; C07D409-12; C07D295-15; C07D223-04; C07D209-20; C07C211-10; C07C233-76; C07C233-78; A61K031-495; A61K031-445; A61K031-40; A61K031-55; A61K031-535; A61K031-475; A61K031-505; A61K031-44; A61K031-165
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 34
ST indole nonpeptide tachykinin receptor antagonist prepn
IT Analgesics
Antidepressants
Anxiolytics
(prepn. of non-peptide tachykinin receptor antagonists)
IT Down's syndrome
Multiple sclerosis
Psoriasis
Schizophrenia
(treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Mental disorder
(Alzheimer's disease, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Respiratory distress syndrome
(adult, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Inflammation inhibitors
(antiarthritics, prepn. of non-peptide tachykinin receptor antagonists)
IT Bronchodilators
(antiasthmatics, prepn. of non-peptide tachykinin receptor antagonists)
IT Tranquilizers and Neuroleptics
(antipsychotics, prepn. of non-peptide tachykinin receptor antagonists)
IT Inflammation inhibitors
(antirheumatics, prepn. of non-peptide tachykinin receptor antagonists)
IT Pneumonia
(broncho-, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Mental disorder
(dementia, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Nervous system
(disease, amyotrophic lateral sclerosis, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Connective tissue
(disease, fibrositis, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Bladder
(disease, incontinence, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Bronchi
(diseases, spasm, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Intestine, disease
(irritable bowel syndrome, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Kinins (animal hormones)
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(neuro-, prepn. of non-peptide tachykinin receptor antagonists)
IT Brain, disease
(stroke, treatment; prepn. of non-peptide tachykinin receptor antagonists)
IT Kinin receptors
Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinin, prepn. of non-peptide tachykinin receptor antagonists)
IT Kinin receptors
Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinin NK1, prepn. of non-peptide tachykinin receptor antagonists)
IT Kinin receptors
Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinin NK2, prepn. of non-peptide tachykinin receptor antagonists)
IT Kinins (animal hormones)
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinins, prepn. of non-peptide tachykinin receptor antagonists)
IT 170568-24-8P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct; prepn. of non-peptide tachykinin receptor antagonists)
IT 170567-77-8P
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation)
(byproduct; prepn. of non-peptide tachykinin receptor antagonists)
IT 47738-79-4P 170568-11-3P 170568-12-4P 170568-13-5P
170568-14-6P 170568-15-7P 170568-16-8P 170568-17-9P
170568-18-0P 170568-19-1P 170568-20-4P 170568-21-5P
170568-22-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of non-peptide tachykinin receptor antagonists)
IT 170566-34-4P 170566-35-5P 170566-36-6P 170566-37-7P
170566-38-8P 170566-39-9P 170566-40-2P 170566-41-3P
170566-42-4P 170566-43-5P 170566-44-6P 170566-45-7P
170566-46-8P 170566-47-9P 170566-48-0P 170566-49-1P
170566-50-4P 170566-51-5P 170566-52-6P 170566-53-7P
170566-54-8P 170566-55-9P 170566-56-0P 170566-57-1P
170566-58-2P 170566-59-3P 170566-60-6P 170566-61-7P
170566-62-8P 170566-63-9P 170566-64-0P 170566-65-1P
170566-66-2P 170566-67-3P 170566-68-4P 170566-69-5P
170566-70-8P 170566-71-9P 170566-72-0P 170566-73-1P
170566-74-2P 170566-75-3P 170566-76-4P 170566-77-5P
170566-78-6P 170566-79-7P 170566-80-0P 170566-81-1P
170566-82-2P 170566-83-3P 170566-84-4P 170566-85-5P
170566-86-6P 170566-87-7P 170566-88-8P 170566-89-9P
170566-90-2P 170566-91-3P 170566-92-4P 170566-93-5P
170566-94-6P 170566-95-7P 170566-96-8P 170566-97-9P
170566-98-0P 170566-99-1P 170567-00-7P 170567-01-8P
170567-02-9P 170567-03-0P 170567-04-1P 170567-05-2P

170567-06-3P 170567-07-4P 170567-08-5P 170567-09-6P
170567-10-9P 170567-11-0P 170567-12-1P 170567-13-2P
170567-14-3P 170567-15-4P 170567-16-5P 170567-17-6P
170567-18-7P 170567-19-8P 170567-20-1P 170567-21-2P
170567-22-3P 170567-23-4P 170567-24-5P 170567-25-6P
170567-26-7P 170567-27-8P 170567-28-9P 170567-29-0P
170567-30-3P 170567-31-4P 170567-32-5P 170567-33-6P
170567-34-7P 170567-35-8P 170567-36-9P 170567-37-0P
170567-38-1P 170567-39-2P 170567-40-5P 170567-41-6P
170567-42-7P 170567-43-8P 170567-44-9P 170567-45-0P
170567-46-1P 170567-47-2P 170567-48-3P 170567-49-4P
170567-50-7P 170567-51-8P 170567-52-9P 170567-53-0P
170567-54-1P 170567-55-2P 170567-56-3P 170567-57-4P
170567-58-5P 170567-59-6P 170567-60-9P 170567-61-0P
170567-62-1P 170567-63-2P 170567-64-3P 170567-65-4P
170567-66-5P 170567-67-6P 170567-68-7P 170567-69-8P
170567-70-1P 170567-71-2P 170567-72-3P 170567-73-4P
170567-74-5P 170567-75-6P 170567-76-7P 170567-77-8P
170567-78-9P 170567-79-0P 170567-80-3P 170567-81-4P
170567-82-5P 170567-83-6P 170567-84-7P 170567-85-8P
170567-86-9P 170567-87-0P 170567-88-1P 170567-89-2P
170567-90-5P 170567-91-6P 170567-92-7P 170567-93-8P
170567-94-9P 170567-95-0P 170567-96-1P 170567-97-2P
170567-98-3P 170567-99-4P 170568-00-0P 170568-01-1P
170568-02-2P 170568-03-3P 170568-04-4P 170568-05-5P
170568-06-6P 170568-07-7P 170568-08-8P 170568-09-9P
170568-10-2P 170568-25-9P 170568-26-0P 170568-27-1P
170568-28-2P 170568-29-3P 170568-30-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of non-peptide tachykinin receptor antagonists)

IT 76-83-5, Trityl chloride 89-98-5, 2-Chlorobenzaldehyde 135-02-4, 2-Methoxybenzaldehyde 541-41-3, Ethyl chloroformate 598-21-0, Bromoacetyl bromide 624-83-9, Methyl isocyanate 6720-02-1, Tryptophan amide 6850-57-3, 2-Methoxybenzylamine 13139-14-5 17766-28-8, 1-Cyclohexylpiperazine 24424-99-5, Di-tert-butyl dicarbonate 119378-70-0 170568-23-7 170568-31-7 170568-32-8
RL: RCT (Reactant)
(starting material; prepn. of non-peptide tachykinin receptor antagonists)

L17 ANSWER 17 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 123:306600 MARPAT
TI Antithrombotic L-arginine aldehyde derivatives
IN Chirgadze, Nickolay Yuri; Schacht, Aaron Leigh; Smith, Gerald Floyd; Willey, Michael Robert
PA Lilly, Eli, and Co., USA
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
PI WO 9523608 A1 950908
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-US2552 950303
PRAI US 94-207491 940304
DT Patent

LA English

AB L-arginine aldehyde derivs. XYNHCH(CHO)(CH2)3NHC(:NH)NH2 [X = prolyl, homoprolyl, substituted cycloalkylalkanoyl, (substituted) isoquinolinecarbonyl, etc.; Y = substituted prolyl] are prepd. for use as thrombin inhibitors, coagulation inhibitors, and thromboembolic disorder agents. Thus, the plasma thrombin time in rats was doubled by D-homoprolyl-L-cis-4-methylprolyl-L-argininal-2HCl (I) at 60 ng/mL. I was prepd. by stepwise condensation of Cbz-D-homoproline, 4-cis-methylproline Et ester (prepd. from Cbz-4-trans-Hyp Et ester), and Arg(Cbz) lactam-2HCl [prepd. from Boc-Arg(Cbz)], redn. with LiAl(OCMe3)3, and hydrogenolysis over Pd/C.

IC ICM A61K038-00
ICS C07K005-00; C07K007-00; C07K017-00; C07D223-16; C07D251-00; C07D251-40; C07D239-00; C07D237-00; C07D471-00; C07D487-00; C07D417-00; C07D285-00; C07D513-00; C07D285-08; C07D285-14; C07D277-04; C07D277-18; C07D277-38; C07D275-02

CC 1-8 (Pharmacology)
Section cross-reference(s): 34

ST argininal deriv prepn antithrombotic

IT Anticoagulants and Antithrombotics
(antithrombotic arginine aldehyde derivs.)

IT 169819-73-2P 169819-74-3P 169819-75-4P 169819-76-5P
169819-77-6P 169819-78-7P 169819-79-8P 169819-80-1P
169819-81-2P 169819-82-3P 169819-83-4P 169819-84-5P
169819-85-6P 169819-86-7P 169819-87-8P 169819-88-9P
169819-89-0P 169819-90-3P 169819-91-4P 169819-92-5P
169819-93-6P 169819-94-7P 169819-95-8P 169819-96-9P
169819-97-0P 169819-98-1P 169819-99-2P 169820-00-2P
169820-01-3P 169820-02-4P 169820-03-5P 169820-04-6P
169820-05-7P 170078-99-6P 170079-00-2P 170079-01-3P
170207-48-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antithrombotic arginine aldehyde derivs.)

IT 51-35-4 94-18-8, Benzyl 4-hydroxybenzoate 99-06-9, 3-Hydroxybenzoic acid, reactions 100-02-7, 4-Nitrophenol, reactions 100-39-0, Benzyl bromide 108-95-2, Phenol, reactions 486-73-7, 1-Isoquinolinecarboxylic acid 554-84-7 673-06-3, D-Phenylalanine 883-40-9, Diphenyldiazomethane 1530-32-1, Ethyltriphenylphosphonium bromide 1723-00-8, D-Homoproline 1779-49-3, Methyltriphenylphosphonium bromide 5292-43-3, tert-Butyl bromoacetate 6228-47-3, Propyltriphenylphosphonium bromide 13504-85-3 16721-45-2 18942-49-9, BOC-D-phenylalanine 28322-40-9, Isoamyltriphenylphosphonium bromide 33125-05-2 35897-34-8 79815-20-6, (S)-Indoline-2-carboxylic acid 93967-76-1 169820-89-7
RL: RCT (Reactant)
(antithrombotic arginine aldehyde derivs.)

IT 28697-09-8P 33996-30-4P 51219-18-2P 51219-20-6P 77513-40-7P
83507-89-5P 84052-82-4P 89083-53-4P 103667-57-8P
103733-65-9P 169390-26-5P 169390-27-6P 169820-06-8P
169820-07-9P 169820-08-0P 169820-09-1P 169820-10-4P
169820-11-5P 169820-12-6P 169820-13-7P 169820-14-8P
169820-15-9P 169820-16-0P 169820-17-1P 169820-18-2P
169820-19-3P 169820-20-6P 169820-21-7P 169820-22-8P
169820-23-9P 169820-24-0P 169820-25-1P 169820-26-2P
169820-27-3P 169820-28-4P 169820-29-5P 169820-30-8P
169820-31-9P 169820-32-0P 169820-33-1P 169820-34-2P

169820-35-3P 169820-36-4P 169820-37-5P 169820-38-6P
169820-39-7P 169820-40-0P 169820-41-1P 169820-42-2P
169820-43-3P 169820-44-4P 169820-45-5P 169820-46-6P
169820-47-7P 169820-48-8P 169820-49-9P 169820-50-2P
169820-51-3P 169820-52-4P 169820-53-5P 169820-54-6P
169820-55-7P 169820-56-8P 169820-57-9P 169820-58-0P
169820-59-1P 169820-60-4P 169820-61-5P 169820-62-6P
169820-63-7P 169820-64-8P 169820-65-9P 169820-66-0P
169820-67-1P 169820-68-2P 169820-69-3P 169820-70-6P
169820-71-7P 169820-72-8P 169820-73-9P 169820-74-0P
169820-75-1P 169820-76-2P 169820-77-3P 169820-78-4P
169820-79-5P 169820-80-8P 169820-81-9P 169820-82-0P
169820-83-1P 169820-84-2P 169820-85-3P 169820-86-4P
169820-87-5P 169820-88-6P 170079-02-4P 170079-03-5P
170079-04-6P 170079-05-7P 170079-06-8P 170079-07-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(antithrombotic arginine aldehyde derivs.)

IT 9002-04-4, Thrombin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; antithrombotic arginine aldehyde derivs.)

L17 ANSWER 18 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 123:279761 MARPAT
TI Hydroxyethylamino sulfonamides useful as retroviral protease inhibitors
IN Vazquez, Michael L.; Mueller, Richard A.; Talley, John J.; Getman, Daniel P.; Decrescenzo, Gary A.; Freskos, John N.; Bertenshaw, Deborah E.; Heintz, Robert M.
PA Searle, G. D., and Co., USA; Monsanto Co.
SO PCT Int. Appl., 255 pp.
CODEN: PIXXD2
PI WO 9506030 A1 950302
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, US, UZ, VN
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 94-US9139 940823
PRAI US 93-110911 930824
US 94-204827 940302
DT Patent
LA English
AB Hyroxethylamino sulfonamide compds. AC(:Y)NR6CHR2CHOHCH2NR3S(:O)xR4 [I: R2=(substituted)alkyl, aryl, cycloalkyl, cycloalkylalkyl, aralkyl; R3=H; R3,R4=R2, alkenyl, alkynyl, heterocycloalkyl, -aryl, -aralkyl, -cycloalkyalkyl; R6=H, alkyl; x=1,2; Y=O, S; A=RO, R; R=alkyl, alkenyl; (hetero)aryl, cycloalkyl, cycloalkylalkyl, aralkyl, NH2, mono- or disubstituted amino, etc.] are effective as retroviral protease inhibitors, and in particular as inhibitors of HIV protease. Many inhibitors were prepd. by (1) prepg. an N-protected amino epoxide and (2) reacting this with an amine and (3) prepg. a sulfonamide by reacting with a sulfonyl chloride or sulfonyl anhydride in the presence of an acid scavenger. The amino function of the sulfonamide was then (4) deprotected and (5) reacted with a carboxylate. In vitro HIV protease assays with these compds. revealed inhibitors with IC50's as low as 1.4 nM, e.g. [1S-[1R*(S*),2S*]]-I (A=p-MeOC6H4CH2OCONHCH2CHMe; Y=O; R6=H; R2=benzyl; R3=3-methylbutyl; x=2; R4=phenyl).
IC ICM C07C311-29

ICS C07D213-30; C07C317-14; C07C311-18; C07D307-79; C07K005-062; A61K031-18; A61K031-44
CC 7-3 (Enzymes)
ST retrovirus protease inhibitor hydroxyethylamino sulfonamide; HIV protease inhibitor hydroxyethylamino sulfonamide
IT 144114-21-6, Retropepsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV; hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)
IT 169280-63-1P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)
IT 1975-51-5P, 4-Nitro-2-methylbenzoic acid 157445-94-8P
157566-75-1P 157566-99-9P 157567-06-1P 159005-60-4P
159005-62-6P 159005-67-1P 159005-68-2P 159005-69-3P
159005-70-6P 159005-74-0P 159005-75-1P 159005-76-2P
159005-77-3P 159005-78-4P 159005-79-5P 159005-80-8P
159005-81-9P 159005-82-0P 159005-83-1P 159005-84-2P
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159005-99-9P 159006-00-5P 159006-01-6P 159006-02-7P
159006-03-8P 159006-07-2P 159006-19-6P 159006-21-0P
159006-23-2P 159006-24-3P 159006-25-4P 159006-26-5P
159006-27-6P 159006-28-7P 159006-29-8P 159006-30-1P
159006-31-2P 159006-32-3P 159006-33-4P 159006-34-5P
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161721-81-9P 169280-35-7P 169280-38-0P 169280-39-1P
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169280-44-8P 169280-45-9P 169280-46-0P 169280-47-1P
169280-48-2P 169280-49-3P 169280-50-6P 169280-51-7P
169280-52-8P 169280-53-9P 169280-54-0P 169280-55-1P
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169280-69-7P 169280-70-0P 169280-71-1P 169280-72-2P
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169280-77-7P 169280-78-8P 169280-93-7P 169280-94-8P
169280-95-9P 169280-96-0P 169280-97-1P 169280-98-2P
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169281-03-2P 169281-04-3P 169281-05-4P 169281-06-5P
169281-07-6P 169281-08-7P 169281-09-8P 169281-10-1P
169281-11-2P 169281-12-3P 169281-13-4P 169281-14-5P
169281-15-6P 169281-16-7P 169281-17-8P 169436-99-1P
169437-00-7P 169437-01-8P 169437-02-9P 169437-03-0P
169437-04-1P 169437-05-2P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)
IT 62-56-6, Thiourea, reactions 63-91-2, L-Phenylalanine, reactions 74-89-5, Methylamine, reactions 75-77-4, reactions 78-81-9, Isobutylamine 79-08-3, Bromoacetic acid 79-37-8, Oxalyl chloride 87-62-7, 2,6-Dimethylaniline 95-48-7, reactions 96-34-4, Methyl

chloroacetate 98-09-9, Benzenesulfonyl chloride 98-68-0, 4-Methoxybenzenesulfonyl chloride 98-74-8, 4-Nitrobenzene sulfonyl chloride 100-39-0, Benzyl bromide 100-55-0, 3-Pyridylcarbinol 105-13-5, 4-Methoxybenzyl alcohol 105-36-2, Ethyl bromoacetate 107-31-3, Methyl formate 107-85-7, Isoamylamine 121-51-7, 3-Nitrobenzene sulfonyl chloride 124-63-0, Methanesulfonyl chloride 274-09-9, 1,3-Benzodioxole 496-16-2, 2,3-Dihydrobenzofuran 506-59-2, Dimethylamine hydrochloride 541-88-8, Chloroacetic anhydride 576-26-1 603-80-5, 3-Hydroxy-2-methylbenzoic acid 619-45-4, Methyl p-aminobenzoate 632-46-2, 2,6-Dimethylbenzoic acid 933-88-0, o-Toluoyl chloride 1118-68-9, N,N-Dimethylglycine 2170-03-8, Itaconic anhydride 2304-96-3, N-Carbobenzoxy-L-asparagine 3167-49-5, 6-Aminonicotinic acid 3182-95-4, L-Phenylalaninol 3391-99-9 3392-08-3 4412-91-3, 3-(Hydroxymethyl)furan 5006-66-6, 6-Hydroxynicotinic acid 5326-38-5, 2-Iodo-5-nitrotoluene 10147-36-1, Propanesulfonyl chloride 18162-48-6, tert-Butyldimethylsilyl chloride 22118-09-8, Bromoacetyl chloride 23326-27-4, Methyl tetrolate 24424-99-5, Di-tert-butyldicarbonate 25193-95-7, 5-Pyrimidinemethanol 25512-62-3, Cyclohexenone 26049-94-5 30925-18-9 39178-35-3, Isonicotinoyl chloride hydrochloride 52130-17-3, 3-Amino-2-methylbenzoic acid 62965-10-0 74124-79-1, N,N'-Disuccinimidyl carbonate 79107-75-8 103095-36-9 128018-44-0 136465-99-1 138499-08-8 143224-62-8 157445-95-9 157566-95-5 157567-10-7 159005-61-5 159005-92-2 159006-06-1 159006-48-1
RL: RCT (Reactant)
(hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

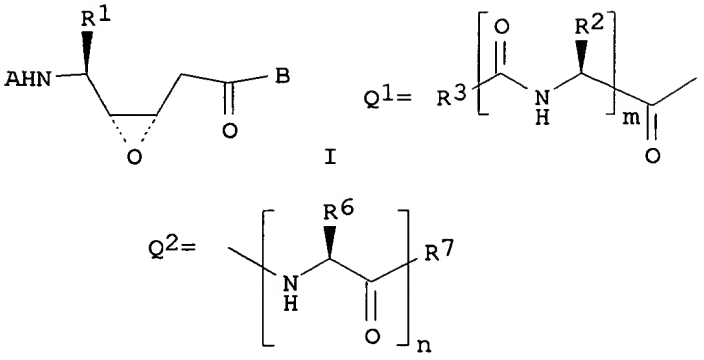
IT 93-85-6P, 2-Amino-6-carboxybenzothiazole 578-39-2P, 4-Hydroxy-2-methylbenzoic acid 1878-49-5P, 2-Methylphenoxyacetic acid 3377-31-9P 6633-61-0P, Methyl 2-aminothiazole-5-carboxylate 13335-71-2P, 2,6-Dimethylphenoxyacetic acid 14527-44-7P, Methyl 5-thiazolecarboxylate 38585-74-9P, 5-Thiazolemethanol 39658-41-8P, Ethyl 6-aminonicotinate 50850-93-6P 54781-19-0P, 2-Trimethylsilyloxy-1,3-cyclohexadiene 60427-77-2P 83509-04-0P 84575-50-8P 111060-52-7P 111060-64-1P 115010-10-1P, 1,3-Benzodioxole-5-sulfonyl chloride 115010-11-2P 127927-43-9P 127943-39-9P 128018-43-9P 130165-86-5P 132605-93-7P 132605-97-1P 132605-98-2P 132696-45-8P 143224-86-6P 143225-04-1P 157446-10-1P 157566-90-0P 157566-91-1P 157567-12-9P 157567-13-0P 159005-59-1P 159005-71-7P 159005-90-0P 159006-04-9P 159006-05-0P 159006-08-3P 159006-09-4P 159006-10-7P 159006-11-8P 159006-12-9P 159006-13-0P 159006-14-1P 159006-15-2P 159006-16-3P 159006-17-4P 159006-18-5P 159006-20-9P 159006-22-1P 169280-79-9P 169280-80-2P 169280-81-3P 169280-82-4P 169280-83-5P 169280-84-6P 169280-85-7P 169280-86-8P 169280-87-9P 169280-88-0P 169280-89-1P 169280-90-4P 169280-91-5P 169280-92-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(hydroxyethylamino sulfonamides useful as retroviral protease inhibitors)

L17 ANSWER 19 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 123:169940 MARPAT
TI Enzymic reduction method for the preparation of compounds useful for preparing taxanes
IN Patel, Ramesh N.; Banerjee, Amit; McNamee, Clyde G.; Thottathil, John K.; Szarka, Laszlo J.

PA Squibb, E. R., and Sons, Inc., USA
SO U.S., 13 pp.
CODEN: USXXAM
PI US 5420337 A 950530
AI US 92-975453 921112
DT Patent
LA English
OS CASREACT 123:169940
AB RR1CHCOCO2R2 [R = aryl; R1 = (un)protected NH2, N3; R2 = H, alkyl, aryl, cycloalkyl, alkenyl, alkynyl, cycloalkenyl] were prepd. as substartes for enzymic redn. in the prepn. of intermediates for the taxane side chain. Thus, DL-H2NCHPhCO2H was N-benzoylated, treated with EtO2CCOCl, and hydrolyzed to give (.+-.)-BzNHCHPhCOCO2Et which was reduced with Hansenula polymorpha to give (2R,3S)-(-)-BzNHCHPhCH(OH)CO2Et in 98% yield with 99.5% optical purity.
IC ICM C07C229-28
NCL 560041000
CC 30-20 (Terpenes and Terpenoids)
Section cross-reference(s): 34
ST benzoylphenylisoserine enzymic stereoselective prepn; taxane intermediate benzoylphenylisoserine enzymic prepn; bezoylaminooxophenylpropionate stereoselective redn Hansenula
IT Hansenula polymorpha
(stereoselective prepn. of the taxane side chain intermediates by enzymic redn.)
IT Reduction
(enzymic, stereoselective prepn. of the taxane side chain intermediates by enzymic redn.)
IT 1605-68-1P, Taxane 33069-62-4P, Taxol
RL: PNU (Preparation, unclassified); PREP (Preparation)
(stereoselective prepn. of the taxane side chain intermediates by enzymic redn.)
IT 2835-06-5, DL-Phenylglycine
RL: RCT (Reactant)
(stereoselective prepn. of the taxane side chain intermediates by enzymic redn.)
IT 28065-66-9P, DL-N-Benzoylphenylglycine 167095-12-7P 167095-13-8P 167095-14-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(stereoselective prepn. of the taxane side chain intermediates by enzymic redn.)
IT 153433-80-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective prepn. of the taxane side chain intermediates by enzymic redn.)

L17 ANSWER 20 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 123:9927 MARPAT
TI Preparation of cis-epoxide peptide derivatives useful as irreversible HIV protease inhibitors.
IN Kim, Sung Chun; Choy, Nakyen; Lee, Chang Sun; Son, Young Chan; Choi, Hoil; Koh, Jong Sung; Yoon, Heungsik; Park, Chi Hyo; Kim, Sang Soo
PA Lucky Ltd., S. Korea
SO Eur. Pat. Appl., 95 pp.
CODEN: EPXXDW
PI EP 601486 A1 940615
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
AI EP 93-119458 931202
PRAI KR 92-23088 921202

KR 92-23089 921202
KR 93-10811 930614
KR 93-21298 931014
KR 93-21299 931014
KR 93-21300 931014
DT Patent
LA English
GI



AB Title compds. [I; R1 = cycloalkyl, arylalkyl; A = Q1; R2 = (amide-substituted) alkyl; R3 = alkoxy, aryloxyalkyl, arylalkoxy, N-contg. arom. radical, N-contg. arom. radical-substituted alkoxy, amino; B = Q2; R6 = alkyl, aralkyl, amide-substituted alkyl; R7 = alkoxy, alkylamino, alkoxyamino, dialkylamino, etc.; m = 0,1; n = 1,2], were prepd. Thus, N-[5-L-(N-benzyloxycarbonylamino)-(4R,3S)-epoxy-6-phenylhexanoyl]isoleucine Me ester (prepn. given) was hydrogenolyzed in MeOH over Pd/C; the residue was coupled with N-(2-quinolinecarbonyl)asparagine using EDC/HOBT/Et3N in DMF to give N-[5-L-[[N-(2-quinolinecarbonyl)asparaginyl]amino]epoxy-6-phenylhexanoyl]isoleucine Me ester. The latter inhibited HIV protease with KI = 0.018 .mu.M, and inhibited HIV proliferation in cell culture with IC50 = 0.2 .mu.M.

IC ICM C07K005-02
ICS C07K007-02; C07K005-06; C07D303-36; C07D303-46; A61K037-64; A61K031-335; C07C271-20; C07C271-22; C07D303-38; C07D493-08
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST peptide epoxide prepn hiv protease inhibitor
IT Virucides and Virustats
(epoxypeptide derivs., for HIV infections)
IT Virus, animal
(human immunodeficiency, infection by, treatment of, epoxypeptide derivs. for)
IT 144114-21-6, Retropepsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(HIV, inhibitors, epoxypeptide derivs.)
IT 160742-15-4P 160742-16-5P 160742-17-6P 160742-18-7P
160742-19-8P 160742-20-1P 160742-21-2P 160742-22-3P
160742-23-4P 160742-24-5P 160742-25-6P 160742-26-7P
160742-27-8P 160742-28-9P 160742-29-0P 160742-30-3P

160742-31-4P 160742-32-5P 160742-33-6P 160742-34-7P
160742-35-8P 160742-36-9P 160742-37-0P 160742-38-1P
160742-39-2P 160742-40-5P 160742-41-6P 160742-42-7P
160742-89-2P 160742-96-1P 160742-97-2P 160742-98-3P
160742-99-4P 160743-00-0P 160743-01-1P 160743-02-2P
160743-03-3P 160743-04-4P 160743-05-5P 160743-06-6P
160743-07-7P 160743-08-8P 160743-09-9P 160743-10-2P
160743-11-3P 160743-12-4P 160743-13-5P 160743-14-6P
160743-15-7P 160743-16-8P 160743-17-9P 160743-18-0P
160743-19-1P 160743-20-4P 160743-21-5P 160743-22-6P
160743-23-7P 160743-24-8P 160743-25-9P 160743-26-0P
160743-27-1P 160743-28-2P 160743-29-3P 160743-30-6P
160743-31-7P 160743-32-8P 160743-33-9P 160743-34-0P
160743-35-1P 160743-36-2P 160743-37-3P 160743-38-4P
160743-39-5P 160743-40-8P 160743-41-9P 160743-42-0P
160743-43-1P 160743-44-2P 160743-45-3P 160743-46-4P
160743-47-5P 160743-48-6P 160743-49-7P 160743-50-0P
160743-51-1P 160743-52-2P 160743-53-3P 160743-54-4P
160865-35-0P 160865-36-1P 160865-37-2P 160865-40-7P
160865-41-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as HIV protease inhibitor)

IT 1828-66-6P, 4-Morpholinesulfonyl chloride 4083-58-3P 7484-37-9P
21035-59-6P 35909-92-3P 51600-25-0P 51987-73-6P 58521-45-2P
59830-60-3P 63096-02-6P 65273-64-5P 68906-27-4P 72155-45-4P
84541-20-8P 97589-56-5P 101669-42-5P 128647-51-8P
134807-20-8P 134807-31-1P 144163-45-1P 156641-81-5P
156641-83-7P 156641-84-8P 156641-85-9P 156641-86-0P
156641-87-1P 156715-06-9P 160742-43-8P 160742-44-9P
160742-45-0P 160742-46-1P 160742-47-2P 160742-48-3P
160742-49-4P 160742-50-7P 160742-51-8P 160742-52-9P
160742-53-0P 160742-54-1P 160742-55-2P 160742-56-3P
160742-57-4P 160742-58-5P 160742-59-6P 160742-61-0P
160742-62-1P 160742-63-2P 160742-64-3P 160742-65-4P
160742-66-5P 160742-67-6P 160742-68-7P 160742-69-8P
160742-70-1P 160742-71-2P 160742-72-3P 160742-73-4P
160742-74-5P 160742-75-6P 160742-76-7P 160742-77-8P
160742-78-9P 160742-79-0P 160742-80-3P 160742-81-4P
160742-82-5P 160742-83-6P 160742-84-7P 160742-85-8P
160742-86-9P 160742-87-0P 160742-88-1P 160742-89-2P
160742-90-5P 160742-94-9P 160742-95-0P 160865-38-3P
160865-42-9P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as intermediate for HIV protease inhibitor)

IT 56-41-7, Alanine, reactions 63-91-2, Phenylalanine, reactions
74-89-5, Methylamine, reactions 78-82-0, Isobutyronitrile
93-10-7, 2-Quinolinecarboxylic acid 100-02-7, 4-Nitrophenol, reactions 100-59-4 574-98-1, N-(2-Bromoethyl)phthalimide
586-98-1, 2-Pyridinecarbinol 637-59-2, 1-Bromo-3-phenylpropane
676-58-4, Methylmagnesium chloride 1121-60-4,
2-Pyridinecarboxaldehyde 1142-20-7, Z-Ala-OH 1149-26-4, Z-Val-OH
1152-61-0, Z-Asp-OH 1462-75-5, 3-Phenylpropylmagnesium bromide
1589-82-8, Benzylmagnesium bromide 2304-96-3, Z-Asn-OH
2577-46-0, Isoleucine methyl ester 2650-64-8, Z-Gln-OH
2976-75-2, 1-Naphthoxyacetic acid 3160-59-6, Z-Ile-OH 3277-89-2,
2-Phenylethylmagnesium bromide 4497-04-5, 4-Morpholinepropanoic acid 5680-86-4 13139-15-6, BOC-Leu-OH 13734-34-4, BOC-Phe-OH
17609-47-1, Valine ethyl ester hydrochloride 42807-91-0

52103-13-6 54745-92-5, Quinoxaline-2-carbonyl chloride
63096-02-6 70240-41-4 90878-19-6 105852-47-9 126456-43-7
136465-98-0 160742-91-6 160742-92-7 160742-93-8 160865-39-4
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(reaction of, in prepn. of epoxypeptide deriv. HIV protease inhibitor)

L17 ANSWER 21 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 122:82085 MARPAT
TI Preparation of acyclic peptides as cardiovascular agents (natriuretics).
IN Voges, Klaus Peter; Henning, Rolf; Huebsch, Walter; Lenfers, Jan Bernd; Beuck, Martin; Theiss, Gudrun; Stasch, Johannes Peter; Hirth-Dietrich, Claudia
PA Bayer A.-G., Germany
SO Ger. Offen., 73 pp.
CODEN: GWXXBX
PI DE 4242946 A1 940623
AI DE 92-4242946 921218
DT Patent
LA German
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB R1COABDEGR2 [A = bond, Q1, Q2, Q3; a, b, d, f = 1,2; e = 0-2; R3, R10, R26 = H, alkyl, protecting group; R4, R5, R11, R12, R27, R28 = H, Me, etc.; R4R5, R11R12 = atoms to form a 5-6 membered carbocycle; B = Q4, Q5, Q6, etc.; j = 0-4; g = 1-3; R9 = H, protecting group; D, E, G = B, Q7; R1 = alkyl, pyridyl, quinolyl, etc.; R2 = Q8; k, l = 0-2; R29, R30 = H, protecting group, (substituted) alkyl], were prepd. as natriuretics (no data). Thus, title compd. (I) was prepd. on Tentagel-S-NH2 resin using FMOC-protected amino acids.
IC ICM C07K007-06
ICS C07K007-02; A61K037-02
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST peptide acyclic prepn natriuretic; cardiovascular agent acyclic peptide prepn
IT Antihypertensives
Cardiovascular agents
(acyclic peptides)
IT Peptides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiovascular agents)
IT Diuretics
(natriuretics, acyclic peptides)
IT 160344-78-5P 160344-79-6P 160344-80-9P 160344-81-0P
160344-82-1P 160344-83-2P 160344-84-3P 160344-85-4P
160344-86-5P 160344-87-6P 160344-88-7P 160344-89-8P
160344-90-1P 160344-91-2P 160344-92-3P 160344-93-4P
160344-94-5P 160344-95-6P 160344-96-7P 160344-97-8P
160344-98-9P 160344-99-0P 160345-00-6P 160345-01-7P
160345-02-8P 160345-03-9P 160345-04-0P 160345-05-1P
160345-06-2P 160345-07-3P 160345-08-4P 160345-09-5P

160345-10-8P 160345-11-9P 160345-12-0P 160345-13-1P
160345-14-2P 160345-15-3P 160345-16-4P 160345-17-5P
160345-18-6P 160345-19-7P 160345-20-0P 160345-21-1P
160345-22-2P 160345-23-3P 160345-24-4P 160345-25-5P
160345-26-6P 160345-27-7P 160345-28-8P 160345-29-9P
160345-30-2P 160345-31-3P 160345-32-4P 160345-33-5P
160345-34-6P 160345-35-7P 160345-36-8P 160345-37-9P
160345-38-0P 160345-39-1P 160345-40-4P 160345-41-5P
160345-42-6P 160345-43-7P 160345-44-8P 160345-45-9P
160345-46-0P 160345-47-1P 160345-48-2P 160345-49-3P
160345-50-6P 160345-51-7P 160345-52-8P 160345-53-9P
160345-54-0P 160345-55-1P 160345-56-2P 160345-57-3P
160345-58-4P 160345-59-5P 160345-60-8P 160345-61-9P
160345-62-0P 160345-63-1P 160345-64-2P 160345-65-3P
160345-66-4P 160345-67-5P 160345-68-6P 160345-69-7P
160345-70-0P 160345-71-1P 160345-72-2P 160345-73-3P
160345-74-4P 160345-75-5P 160345-76-6P 160345-77-7P
160345-78-8P 160345-79-9P 160345-80-2P 160345-81-3P
160345-82-4P 160345-83-5P 160345-84-6P 160345-85-7P
160345-86-8P 160345-87-9P 160345-88-0P 160345-89-1P
160345-90-4P 160345-91-5P 160345-92-6P 160345-93-7P
160345-94-8P 160345-95-9P 160345-96-0P 160345-97-1P
160345-98-2P 160345-99-3P 160346-00-9P 160346-01-0P
160346-02-1P 160346-03-2P 160346-04-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as cardiovascular agent)

IT 68030-63-7P 80897-78-5P 160346-05-4P 160346-06-5P
160346-07-6P 160346-08-7P 160346-09-8P 160346-10-1P
160346-11-2P 160346-12-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for acyclic peptide cardiovascular agent)

IT 96-15-1, 2-Methylbutylamine 2243-83-6, 2-Naphthoyl chloride
2480-93-5, BOC-Orn(Z)-OH 5438-70-0, Ethyl 4-aminophenylacetate
7536-58-5 15761-39-4, BOC-Pro-OH 18598-74-8,
H-Ile-OMe.hydrochloride 71989-14-5, FMOC-Asp(OtBu)-OH
71989-23-6, FMOC-Ile-OH 71989-31-6, FMOC-Pro-OH 109425-55-0,
FMOC-Orn(BOC)-OH
RL: RCT (Reactant)
(reaction of, in prepn. of acyclic peptide cardiovascular agent)

L17 ANSWER 22 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 122:82084 MARPAT
TI Preparation of sulfur-containing peptides as antihypertensives.
IN Voges, Klaus Peter; Henning, Rolf; Lenfers, Jan Bernd; Dressel, Juergen; Beuck, Martin; Theiss, Gudrun; Stasch, Johannes Peter; Hirth-Dietrich, Claudia; Bischoff, Erwin
PA Bayer A.-G., Germany
SO Ger. Offen., 37 pp.
CODEN: GWXXBX
PI DE 4242945 A1 940623
AI DE 92-4242945 921218
DT Patent
LA German
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB R1COABDEGR2 [A = bond, Q1, Q2, Q3; a, b, d, f = 1, 2; e, e' = 0-2; R1 = alkyl, pyridyl, quinolyl, etc.; R3, R10, R19 = H, alkyl, protecting group; R4, R5 = H, Me; or R4 = H, R5 = H, cycloalkyl, aryl, (substituted) alkyl; R4R5C = 5- or 6-membered satd. carbocycle; B = Q4-Q8; g = 1-3; j = 0-4; R9 = H, acyl, protecting group; D, E, G = B, Q9; R11, R12 = R4, R5; R2 = Q10; q, r = 0-2; R20, R21 = R4, R5; R22, R23 = protecting group, H, (substituted) alkyl; .gtoreq. 1 of A, D, E, G = S-contg. amino acid residue, or R1 = S-contg. functional group], were prepd. as antihypertensives (no data). Title compds. are natriuretics with increased affinity for ANP receptors. Thus, title compd. I was prepd. by solid phase synthesis using FMOC-protected amino acids on Tentagel-S-NH2 resin.

IC ICM C07K007-06
ICS A61K037-02; C07K007-02

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST peptide sulfur contg prepn antihypertensive; natriuretic reduced basicity peptide sulfur contg

IT Antihypertensives
(sulfur-contg. peptides)

IT Diuretics
(natriuretics, sulfur-contg. peptides)

IT Peptides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sulfur-contg., prepn. of, as natriuretics)

IT 27144-18-9P 64566-56-9P 81196-09-0P 103725-76-4P
160344-70-7P 160344-71-8P 160344-72-9P 160344-73-0P
160344-74-1P 160344-75-2P 160344-76-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for peptide deriv. natriuretic)

IT 160344-16-1P 160344-17-2P 160344-18-3P 160344-19-4P
160344-20-7P 160344-21-8P 160344-22-9P 160344-23-0P
160344-24-1P 160344-25-2P 160344-26-3P 160344-27-4P
160344-28-5P 160344-29-6P 160344-30-9P 160344-31-0P
160344-32-1P 160344-33-2P 160344-34-3P 160344-35-4P
160344-36-5P 160344-37-6P 160344-38-7P 160344-39-8P
160344-40-1P 160344-41-2P 160344-42-3P 160344-43-4P
160344-44-5P 160344-45-6P 160344-46-7P 160344-47-8P
160344-48-9P 160344-49-0P 160344-50-3P 160344-51-4P
160344-52-5P 160344-53-6P 160344-54-7P 160344-55-8P
160344-56-9P 160344-57-0P 160344-58-1P 160344-59-2P
160344-60-5P 160344-61-6P 160344-62-7P 160344-63-8P
160344-64-9P 160344-65-0P 160344-66-1P 160344-67-2P
160344-68-3P 160344-69-4P 160401-06-9P 160401-07-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as natriuretic)

IT 107-96-0, 3-Mercaptopropionic acid 1197-55-3, p-Aminophenylacetic acid 2462-32-0, Phenylalanine benzyl ester hydrochloride 15761-39-4, BOC-Pro-OH 29022-11-5, FMOC-Gly-OH 71989-14-5, FMOC-Asp(OtBu)-OH 71989-23-6, FMOC-Ile-OH 71989-31-6, FMOC-Pro-OH 103310-88-9 119831-72-0 124815-67-4 160344-77-4
RL: RCT (Reactant)
(reaction of, in prepn. of peptide deriv. natriuretic)

L17 ANSWER 23 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 122:81615 MARPAT
TI Preparation of boronic acids and esters as inhibitors of thrombin

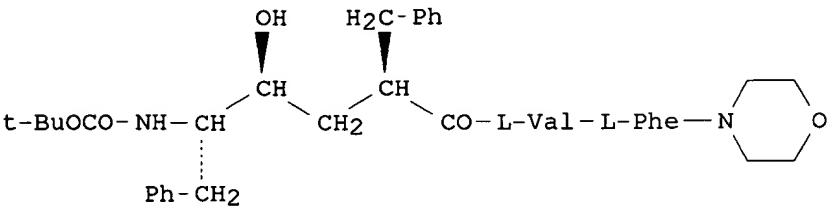
IN Amparo, Eugene Cruz; Miller, William Henry; Pacofsky, Gregory James; Wityak, John
PA Du Pont Merck Pharmaceutical Co., USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
PI WO 9421650 A1 940929
DS W: AU, CA, JP, NZ
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 94-US2965 940323
PRAI US 93-36377 930324
DT Patent
LA English
AB Novel boronic acid derivs. R1ZCNR2BY1Y2 [Y1, Y2 = OH, F, organoamino, C1-8 alkoxy, N, S, O-heteroatom substituted C2-20 cyclic boron ester, etc.; Z = (CH2)mCONR8, (CH2)mCSNR8, (CH2)mSO2NR8, (CH2)mCO2, (CH2)mC(S)O, (CH2)mSO2O, R8 = H, araalkyl, C3-7 cycloalkyl, C1-8 alkyl, m = 0-6; R1 = araalkyl, naphthyl or biphenyl (substituted with one, two, or three substituents selected from halo, cyano, C3-8 cycloalkyl, C2-10 alkenyl), heteroaryl, etc.; R2 = (CH2)nNHC(NH)NH2, (CH2)nNHC(NH)NHAc, (CH2)nSC(NH)NH2, (CH2)nSC(NH2)2, (CH2)nNH(2-pyridyl); n = 3, 4], which are useful inhibitors of trypsin-like enzymes, are disclosed. Thus, N1-(4-phenylbenzoyl)boroarginine (+)-pinanediol bisulfite was prepd. in 4 steps starting from (+)-pinanediol 4-bromo-1(R)-aminobutane-1-boronate. Biol. activity of some of the compds. prepd. is given.
IC ICM C07F005-02
ICS A61K031-69
CC 29-4 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1
ST boronate ester prepn inhibitor thrombin
IT 160195-69-7P 160195-70-0P 160195-71-1P 160195-72-2P
160195-73-3P 160195-74-4P 160195-75-5P 160195-76-6P
160195-77-7P 160195-78-8P 160195-79-9P 160195-80-2P
160195-81-3P 160195-82-4P 160195-83-5P 160195-84-6P
160195-85-7P 160195-86-8P 160195-87-9P 160195-88-0P
160195-89-1P 160195-90-4P 160195-91-5P 160195-92-6P
160195-93-7P 160195-94-8P 160195-95-9P 160195-96-0P
160195-97-1P 160195-98-2P 160195-99-3P 160196-00-9P
160196-01-0P 160196-02-1P 160196-03-2P 160196-04-3P
160196-05-4P 160196-06-5P 160196-07-6P 160196-08-7P
160196-09-8P 160196-10-1P 160196-11-2P 160196-12-3P
160332-87-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of boronic acids and esters as inhibitors of thrombin)
IT 9002-04-4, Thrombin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of boronic acids and esters as inhibitors of thrombin)
IT 62-56-6, Thiourea, reactions 14002-51-8, 4-Phenylbenzoyl chloride 160332-85-4
RL: RCT (Reactant)
(prepn. of boronic acids and esters as inhibitors of thrombin)
IT 160196-13-4P 160196-14-5P 160196-15-6P 160332-86-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of boronic acids and esters as inhibitors of thrombin)

L17 ANSWER 24 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 122:72014 MARPAT

TI Use of inhibitors of HIV proteases for the treatment of tumorous diseases

IN Roesel, Johannes; Regenass, Urs; Lang, Marc; Bold, Guido; Cumin, Frederic
PA Ciba-Geigy A.-G., Switz.

SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
PI EP 626178 A1 941130
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
AI EP 94-810274 940509
PRAI CH 93-1492 930517
DT Patent
LA German
GI



I

AB Inhibitors of HIV (human immunodeficiency virus) aspartate proteinases, and their salts and prodrugs, inhibit the growth of tumors, esp. of those which do not respond directly to inhibition of HIV proteinase. Thus, growth of s.c. transplanted human mammary carcinoma MCF-7 in mice was inhibited by administration twice a day of peptide I (prepn. given) (50 mg/kg orally as aq. soln. contg. 5% DMSO and 20% hydroxypropyl-.beta.-cyclodextrin).

IC ICM A61K037-64
CC 1-6 (Pharmacology)
Section cross-reference(s): 34, 63
ST HIV protease inhibitor antitumor; peptide protease inhibitor antitumor

IT Neoplasm inhibitors
(inhibitors of HIV proteases for treatment of tumorous diseases)

IT Virus, animal
(human immunodeficiency, inhibitors of HIV proteases for treatment of tumorous diseases)

IT 150608-41-6P 150608-56-3P 150736-68-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of HIV proteases for treatment of tumorous diseases)

IT 78169-47-8, Aspartic proteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors of HIV proteases for treatment of tumorous diseases)

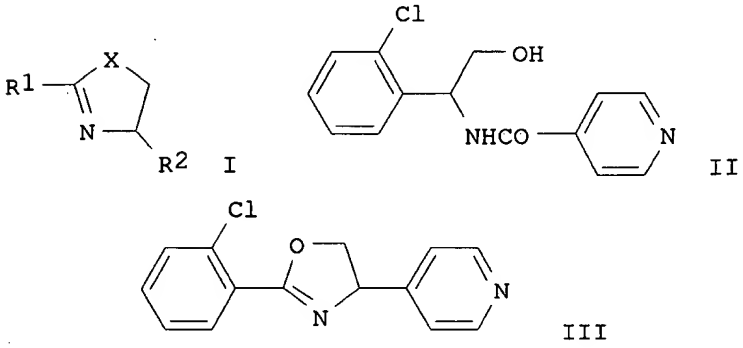
IT 98818-42-9P
RL: BYP (Byproduct); PREP (Preparation)
(inhibitors of HIV proteases for treatment of tumorous diseases)

IT 100-39-0, Benzyl bromide 824-94-2, 4-Methoxybenzyl chloride 2344-80-1, (Chloromethyl)trimethylsilane 18162-48-6 24424-99-5, Boc-anhydride 72155-45-4 113195-57-6, 4-Benzyloxybenzyl iodide 133333-27-4
RL: RCT (Reactant)

(inhibitors of HIV proteases for treatment of tumorous diseases)

IT 70887-29-5P 95977-60-9P 98760-08-8P 98818-41-8P 98818-45-2P
98818-51-0P 107202-43-7P 110600-55-0P 110600-56-1P
112227-09-5P 126410-29-5P 126410-30-8P 135103-86-5P
138498-90-5P 138498-91-6P 141834-13-1P 150609-28-2P
150609-29-3P 151177-18-3P 151920-09-1P 160431-24-3P
160431-25-4P 160431-26-5P 160431-27-6P 160431-28-7P
160431-29-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(inhibitors of HIV proteases for treatment of tumorous diseases)

L17 ANSWER 25 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 121:255787 MARPAT
TI Preparation of thiazoles and oxazoles as insecticides
IN Yamada, Yasuo; Kishimoto, Takashi; Matsuda, Michihiko; Hatano, Renpei; Iwasa, Takao
PA Nippon Soda Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 38 pp.
CODEN: JKXXAF
PI JP 06145169 A2 940524 Heisei
AI JP 93-123547 930427
PRAI JP 92-272452 920917
DT Patent
LA Japanese
OS CASREACT 121:255787
GI



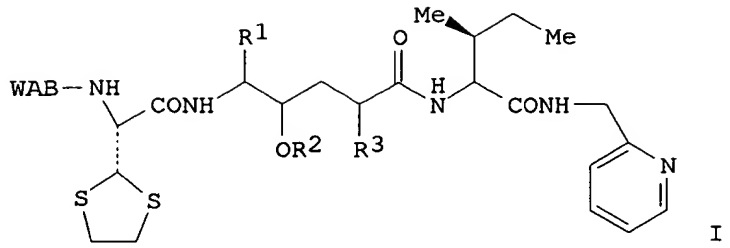
AB The title compds. [I; R1 = (un)substituted heterocyclyl; R2 = (un)substituted Ph, naphthyl, aralkyl, or heterocyclyl], useful as insecticides, are prepd. by (1) cyclization of R1CONHCHR2CH2Y (R1, R2 = same as above; Y = leaving group) or (2) cyclization of R1CONHCHR2CH2Y in the presence of a sulfurization agent. Thus, 0.73 g 2-(2-chlorophenyl)-2-aminoethanol and 1.0 g Et3N were dissolved in THF followed by adding 0.8 g isonicotinoyl chloride hydrochloride under ice-cooling and the resulting mixt. was stirred at room temp. for 12 h, filtered to remove pptd. crystals, and concd. in vacuo to give a residue contg. intermediate (II). This was dissolved in CHCl3 followed by adding 1.2 g SOCl2 and refluxing the resulting mixt. for 2 h and the reaction mixt. was concd. in vacuo, taken up with EtOAc, washed with satd. aq. NaHCO3, dried over anhyd. MgSO4, evapd. in vacuo to give a residue which was dissolved in MeOH followed by adding 2 mL 15% aq. NaOH and heating the resulting mixt. at 70.degree. for 30 min to give, after workup and silica gel chromatog., 0.8 g phenylpyridyloxazole deriv. (III). III sprayed on

cucumber seedlings at 125 ppm killed 100% adult Aphis gossypii vs. 6 and 100% for pyrimicarb and thiometon, resp.
IC ICM C07D413-04
ICS C07D413-04; A01N043-76; A01N043-78; C07D413-14; C07D417-04; C07D417-14
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5
ST thiazole oxazole prepn insecticide; phenylpyridyloxazole prepn insecticide; pyridyloxazole prepn insecticide
IT Insecticides
(prepn. of thiazoles and oxazoles as insecticides)
IT 158499-50-4P 158499-51-5P 158499-52-6P 158499-53-7P
158499-54-8P 158499-55-9P 158499-56-0P 158499-57-1P
158499-58-2P 158499-59-3P 158499-60-6P 158499-61-7P
158499-62-8P 158499-63-9P 158499-64-0P 158499-65-1P
158499-66-2P 158499-67-3P 158499-68-4P 158499-69-5P
158499-70-8P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of thiazoles and oxazoles as insecticides)
IT 39178-35-3, Isonicotinoyl chloride hydrochloride 127428-62-0
RL: RCT (Reactant)
(prepn. of thiazoles and oxazoles as insecticides)
IT 158499-71-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of thiazoles and oxazoles as insecticides)

L17 ANSWER 26 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 120:290102 MARPAT
TI Peptide derivatives for thrombin receptor antagonists
IN Scarborough, Robert M.
PA Cor Therapeutics, Inc., USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
PI WO 9403479 A1 940217
DS W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 93-US6428 930708
PRAI US 92-922340 920730
US 93-80788 930628
DT Patent
LA English
AB Peptide derivs. (Markush included) serving as thrombin receptor antagonists are disclosed, which bear specificity for the cellular thrombin receptor without interfering with the catalytic activities of thrombin. Synthesis of (N,N-di-n-pentyl-Phe)-Cha-Cha-Arg-Lys-NH2 (Cha is cyclohexylalanine) and of other peptides of the invention is described. IC50 values for 60 compds. are included.
IC ICM C07K005-00
ICS C07K007-00; A61K037-02
CC 1-8 (Pharmacology)
ST peptide deriv thrombin receptor antagonist
IT Peptides, biological studies
RL: BIOL (Biological study)
(derivs., for thrombin receptor antagonists)
IT Receptors

RL: BIOL (Biological study)
(thrombin, antagonists of, peptide derivs. for)
IT 9002-04-4, Thrombin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptors, antagonists of, peptide derivs. for)
IT 155115-42-7 155115-43-8 155115-44-9 155115-45-0 155115-46-1
155115-47-2 155115-48-3 155115-49-4 155115-50-7 155115-51-8
155115-52-9 155115-53-0 155115-54-1 155115-55-2 155115-56-3
155115-57-4 155115-58-5 155115-59-6 155115-60-9 155115-61-0
155115-62-1 155115-63-2 155115-64-3 155115-65-4 155115-66-5
155115-67-6 155115-68-7 155115-69-8 155115-70-1 155115-71-2
155115-72-3 155115-73-4 155115-74-5 155115-75-6 155115-76-7
155115-77-8 155115-78-9 155115-79-0 155115-80-3 155115-81-4
155115-82-5 155115-83-6 155115-84-7 155115-85-8 155115-86-9
155115-87-0 155147-19-6 155147-20-9 155147-21-0 155147-22-1
155147-23-2 155147-24-3 155147-25-4 155147-26-5 155147-27-6
155147-28-7 155147-29-8 155147-30-1 155147-31-2 155147-32-3
RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)
(thrombin receptor antagonist activity of)

L17 ANSWER 27 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 120:245787 MARPAT
TI Preparation of dithiolanylglycine containing HIV protease inhibitors of the hydroxyethylene isostere type
IN Haebich, Dieter; Bender, Wolfgang; Hansen, Jutta; Paessens, Arnold
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
PI EP 569811 A1 931118
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
AI EP 93-107140 930503
PRAI DE 92-4215874 920514
DT Patent
LA German
GI



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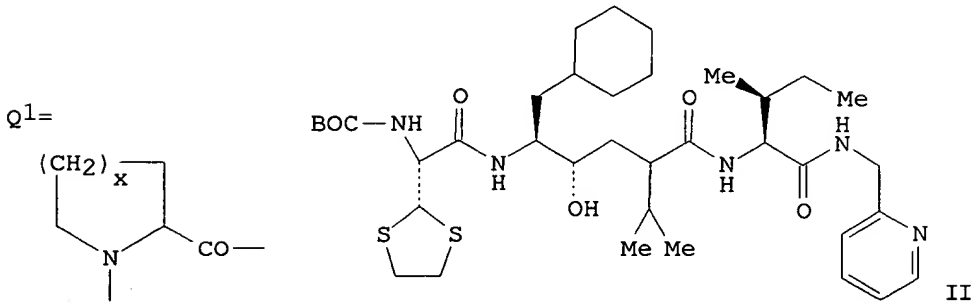


II

AB Title compds. (I; W = H, protecting group, acyl; A, B = bond, NHCMe2CO, Q1, etc.; x = 1, 2; R1 = alkyl substituted by Ph or cyclohexyl; R2 = H, alkyl, protecting group; R3 = alkyl, alkenyl, PhCH2), were prepd. Thus, (2R)-N-(tert-butoxycarbonyl)-2-amino-2-[2-(1,3-dithiolan-2-yl)]acetic acid in CH2Cl2 was stirred with 1-hydroxybenzotriazole/DCC at 0.degree.; 1-[(2R,S,4S,5S)-[5-amino-6-cyclohexyl-4-hydroxy-2-(1-methyl)ethylhexanoyl]]-(S)-isoleucinylpyridylmethylamide dihydrochloride and N-methylmorpholine in CH2Cl2 were added and the mixt. was stirred 2 h at room temp. to give 77% title compd. II. II inhibited HIV-1 protease with IC50 = 1.4 .times.10-9M. I were shown to protect HIV-1 infected cells against virally-induced destruction.

IC ICM C07K005-02
ICS A61K037-64; A61K031-33; C07D409-12; C07D409-14

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST peptide dithiolanylglycyl prepn HIV protease inhibitor; virucide dithiolanylglycyl peptide

IT Virucides and Virustats
(dithiolanylglycyl-contg. peptides, for retroviruses)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of dithiolanylglycyl-contg., as HIV protease inhibitors)

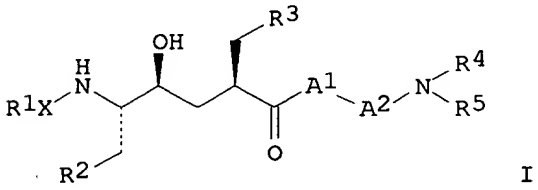
IT 144114-21-6, Retropepsin
RL: RCT (Reactant)
(HIV, inhibitors, dithiolanylglycyl-contg. peptides as)

IT 136520-80-4 137331-84-1 143167-43-5 153625-72-0 153625-73-1
153668-36-1 153668-37-2 153668-43-0
RL: RCT (Reactant)
(coupling reaction of, in prepn. of, as HIV protease inhibitor)

IT 153625-68-4P 153625-69-5P 153625-70-8P 153625-71-9P
153625-72-0P 153625-73-1P 153625-74-2P 153625-75-3P
153625-76-4P 153625-77-5P 153625-78-6P 153625-79-7P
153625-80-0P 153625-81-1P 153668-32-7P 153668-33-8P
153668-34-9P 153668-35-0P 153668-36-1P 153668-37-2P

153668-38-3P 153668-39-4P 153668-40-7P 153668-41-8P
153668-42-9P 153668-44-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as HIV protease inhibitor)

L17 ANSWER 28 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 119:250508 MARPAT
TI Preparation of 5-amino-4-hydroxyhexanoic acid derivative containing peptides as HIV protease inhibitors
IN Lang, Marc; Bold, Guido; Faessler, Alexander; Schneider, Peter; Van Hoogesvest, Peter
PA Ciba-Geigy A.-G., Switz.
SO Eur. Pat. Appl., 79 pp.
CODEN: EPXXDW
PI EP 532466 A2 930317
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
AI EP 92-810678 920903
PRAI CH 91-2689 910912
CH 92-980 920327
CH 92-2007 920625
DT Patent
LA German
GI



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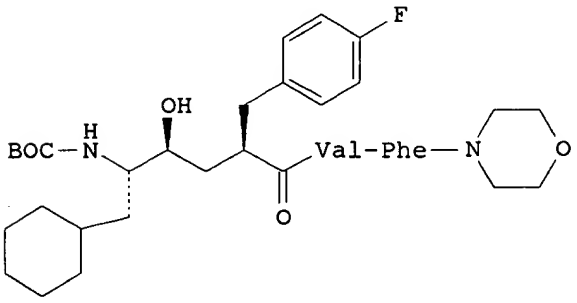

II

AB Title compds. [I; R1 = H, alkoxycarbonyl, heterocyclylcarbonyl, heterocyclyloxycarbonyl, (substituted) benzyloxycarbonyl, etc.; X = bond, .alpha.-amino acid residue; R2, R3 = (substituted) Ph, cyclohexyl; A1 = bond, .alpha.-amino acid residue; A2 = .alpha.-amino acid residue; A1A2 = dipeptide residue whose central amide bond is reduced; NR4R5 = (thio)morpholino], were prepd. as HIV protease inhibitors. Thus, title compd. II was prepd. in many steps starting from BOC-phenylalaninal using soln. phase methods. I inhibited HIV-1 multiplication in MT-2 cells with ED90's of

10-5-10-8M. Generic I oral formulations are given.
IC ICM C07K005-04
ICS C07D295-16; A61K037-64
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST aminohydroxyhexanoate peptide HIV protease inhibitor
IT Virucides and Virustats
(peptides, for HIV)
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 5-amino-4-hydroxyhexanoate-contg., as HIV protease inhibitors)
IT Virus, animal
(human immunodeficiency 1, infection by, treatment of, peptides for)
IT 144114-21-6, Retropepsin
RL: RCT (Reactant)
(HIV; inhibitors, peptide analogs as)
IT 150736-69-9P
RL: FORM (Formation, nonpreparative); SPN (Synthetic preparation); PREP (Preparation)
(formation of, in prepn. of peptide analog HIV protease inhibitor)
IT 150608-20-1P 150608-21-2P 150608-22-3P 150608-23-4P
150608-24-5P 150608-25-6P 150608-26-7P 150608-27-8P
150608-28-9P 150608-29-0P 150608-30-3P 150608-31-4P
150608-32-5P 150608-33-6P 150608-34-7P 150608-35-8P
150608-36-9P 150608-37-0P 150608-38-1P 150608-39-2P
150608-40-5P 150608-41-6P 150608-42-7P 150608-43-8P
150608-44-9P 150608-45-0P 150608-46-1P 150608-47-2P
150608-48-3P 150608-49-4P 150608-50-7P 150608-51-8P
150608-52-9P 150608-53-0P 150608-54-1P 150608-55-2P
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150608-60-9P 150608-61-0P 150608-62-1P 150608-63-2P
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150608-68-7P 150608-69-8P 150608-70-1P 150608-71-2P
150608-72-3P 150608-73-4P 150608-74-5P 150608-75-6P
150608-76-7P 150608-77-8P 150608-78-9P 150608-79-0P
150608-80-3P 150608-81-4P 150608-82-5P 150608-83-6P
150608-84-7P 150608-85-8P 150608-86-9P 150608-87-0P
150608-88-1P 150608-89-2P 150608-90-5P 150608-91-6P
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150609-08-8P 150609-09-9P 150609-10-2P 150609-11-3P
150609-12-4P 150609-13-5P 150609-14-6P 150609-15-7P
150609-16-8P 150609-17-9P 150609-18-0P 150609-19-1P
150736-68-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as HIV protease inhibitor)
IT 1828-66-6P, 4-Morpholinesulfonyl chloride 2835-21-4P
15159-40-7P, 4-Morpholinecarbonyl chloride 16250-37-6P
17543-58-7P 31253-08-4P 41153-30-4P 56414-76-7P 56414-96-1P
78879-20-6P 82611-59-4P 98760-08-8P 98818-41-8P 98818-42-9P
98818-45-2P 98818-51-0P 107202-43-7P 110600-55-0P
110600-56-1P 120125-44-2P 126410-29-5P 126410-30-8P
133333-27-4P 135103-86-5P 135544-90-0P 141834-13-1P
144164-04-5P 149267-74-3P 149296-81-1P 150609-20-4P

150609-21-5P 150609-22-6P 150609-23-7P 150609-24-8P
150609-25-9P 150609-26-0P 150609-27-1P 150609-28-2P
150609-29-3P 150609-30-6P 150609-31-7P 150609-32-8P
150609-33-9P 150609-34-0P 150609-35-1P 150609-36-2P
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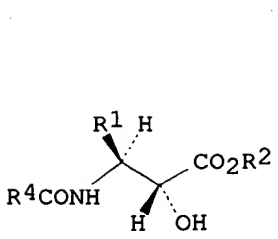
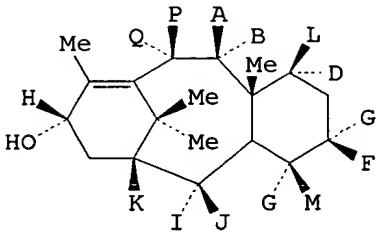
150609-85-1P 150609-86-2P 150609-87-3P 150609-88-4P
150609-89-5P 150609-90-8P 150609-91-9P 150609-92-0P
150609-93-1P 150609-94-2P 150821-06-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for HIV protease inhibitor)

IT 59-67-6, 3-Pyridinecarboxylic acid, reactions 72-18-4, L-Valine, reactions 75-44-5, Carbonic dichloride 105-53-3 107-11-9, 2-Propen-1-amine 109-94-4 123-90-0, Thiomorpholine 459-46-1 535-11-5 1132-68-9 1138-80-3 1149-26-4 1161-13-3 2344-80-1 2462-34-2 3160-59-6 7635-29-2 17201-43-3 19542-51-9 19542-54-2 21760-98-5 26537-68-8, 3-Benzofurancarboxylic acid 72155-45-4 74163-81-8 144163-45-1
RL: RCT (Reactant)
(reaction of, in prepn. of peptide analog HIV protease inhibitor)

L17 ANSWER 29 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 119:249788 MARPAT
TI Synthesis and optical resolution of the taxol side chain and related compounds
IN Peterson, John R.; Zjawiony, Jordan K.; Rogers, Robin D.
PA University of Mississippi, USA
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
PI WO 9310076 A1 930527
DS W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG
AI WO 92-US9911 921119
PRAI US 91-797136 911122
DT Patent
LA English
OS CASREACT 119:249788
GI



I



II

AB Racemic taxane side chain I [R1 = C1-8 linear or branched alkyl, -alkenyl, or -alkynyl, -hydroxyalkyl, C3-8 cycloalkyl or -alkenyl, C5-20 aryl, indolyl, thiophenyl, furanyl, quinolyl, C1-6 aminoalkyl, 2-, 3- or 4-pyridinyl, or UC6H4V (U and V independently = H, halo, OH, SH, NO2, N3, NH2, C2-8-alkyl or -aryl-N-amido, C2-8 alkyl- or arylcarboxylate, etc.); R2 = C1-8 linear or branched alkyl, C3-8 cycloalkyl, C7-12 alkylphenyl; R4 = R1 or OR5; R5 = C1-8 linear or branched alkyl, -alkenyl, or -alkynyl, C3-8-cycloalkyl or -cycloalkenyl, C5-20 aryl] is synthesized and is resolved by crystn., entrainment, or manual sorting due to its conglomerate behavior. The semisynthesis of taxanes (e.g., taxol) via coupling of the substantially optically pure taxane side chain to a taxane ring nucleus II (A or B, P or Q, G or M, and E or F independently = H, lower alkanoyloxy, alkenoyoxy, aroyloxy; AB, PQ, IJ, GM, or EF = O; L and D independently or I, J, or K = H, OH, lower alkanoyloxy, alkenoyloxy, aroyloxy; GM = CH2, oxirane; MF = oxetane) is also described. Thus, the Darzens reaction of PhCHO with ClCH2CO2Me gave 73% (.+-.)-Me trans-3-phenyloxiranecarboxylate (trans-III) which was syn-ring opened by HCl in C6H6 to give 65% (.+-.)-Me threo-3-chloro-2-hydroxy-3-phenylpropionate which in aq. Na2CO3 gave 50% cis-III. Cis-III in MeOH-MeO2CH contg. NaN3, under N, gave 93% (.+-.)-Me threo-3-azido-2-hydroxy-3-phenylpropionate which was etherated with BzCl in CH2Cl2 contg. Et3N and DMAP gave 98% (.+-.)-Me threo-3-azido-2-benzoyloxy-3-phenylpropionate which is hydrogenated in MeOH over Pd/C to give the racemic taxol side chain (.+-.)-N-benzoyl-3-phenylisoserine Me ester [(.+-.)-IV]; the conglomerate nature of this racemate was established crystallog. from the acentric monoclinic P21 space group. (.+-.)-IV was resolved by seed crystal-induced crystn. from EtOH to give (2R,3S)-N-benzoyl-3-phenylisoserine Me ester which was converted to the hydroxy protected O-ethoxyethyl-3-phenylisoserine ester deriv. which was sapond. by aq. methanolic K2CO3 and coupled to 7-triethylsilylbaccatin III followed by HCl deprotection to give taxol.

IC ICM C07C231-20
ICS C07C233-87; C07D305-14; C07C069-675

CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 22, 24, 30, 34, 75

ST optical resoln taxol side chain; crystallog conglomerate taxol side chain resoln

IT Resolution
(of taxol side chain conglomerate)

IT Crystal structure
(of taxol side chain conglomerate and its resolved enantiomorph)

IT Configuration
(abs., of resolved taxol side chain enantiomorph, crystallog. detd.)

IT 96-34-4, Methyl chloroacetate 100-52-7, Benzaldehyde, reactions

RL: RCT (Reactant)
(Darzens reaction of, in conversion to Me phenyloxiranecarboxylate in taxol semisynthesis)

IT 115437-21-3, 7-Triethylsilylbaccatin III
RL: RCT (Reactant)
(coupling of, with taxol side chain enantiomorph, in taxol semisynthesis)

IT 4407-36-7, trans-Cinnamyl alcohol 4510-34-3
RL: RCT (Reactant)
(epoxidn. of)

IT 130607-99-7P, (.+-.)-Methyl cis-3-phenyloxiranecarboxylate
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to Me azido(hydroxy)phenylpropionate in taxol semisynthesis)

IT 98819-67-1P, (.+-.)-trans-3-Phenyloxiranemethanol
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to Me phenyloxiranecarboxylate)

IT 136778-67-1P 136778-69-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and coupling of, with triethylsilylbaccatin III in taxol semisynthesis)

IT 133161-34-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deprotection of, taxol by)

IT 150823-26-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenation/ rearrangement of, in taxol semisynthesis)

IT 32981-85-4P, (2R,3S)-N-Benzoyl-3-phenylisoserine methyl ester
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydroxyl group protection of, in taxol semisynthesis)

IT 105663-44-3P, (.+-.)-cis-3-Phenyloxiranemethanol
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn./esterification of, by sodium periodate and ruthenium trichloride/diazomethane)

IT 145438-00-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ring closure of, in taxol semisynthesis)

IT 136778-73-9P 136779-75-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sapon. of, in taxol semisynthesis)

IT 41603-34-3P, (.+-.)-Methyl trans-3-phenyloxiranecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and syn-ring opening of, in taxol semisynthesis)

IT 129939-46-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and O-benzoylation of, in taxol semisynthesis)

IT 133161-33-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 132074-01-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., crystallog. and resoln. of conglomerate)

IT 109-92-2, Ethyl vinyl ether
RL: RCT (Reactant)
(reaction of, with N-benzoylphenylisoserine Me ester to give O-ethoxyethyl deriv. in taxol semisynthesis)

IT 33069-62-4P, Taxol
RL: PREP (Preparation)
(resoln. of side chain in semisynthesis of)

IT 7782-79-8, Hydrazoic acid
RL: RCT (Reactant)
(ring cleavage of Me phenyloxiranecarboxylate by, in taxol semisynthesis)

L17 ANSWER 30 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 119:226427 MARPAT
TI Peptide aldehydes as antithrombotic agents
IN Balasubramanian, Neelakantan; St. Laurent, Denis R.
PA Bristol-Myers Squibb Co., USA
SO Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW
PI EP 526877 A2 930210
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
AI EP 92-113284 920804
PRAI US 91-741023 910806
DT Patent
LA English
OS CASREACT 119:226427
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Arginine aldehydes I [R1 and R2 = H or COR [R = H, lower alkyl, benzyl, CH(OAc)Me]; R3 and R4 = H, lower alkyl, benzyl, (un)substituted Ph, (un)substituted C3-7 cycloalkyl; R3R4 = (un)substituted C3-7 cycloalkyl; R3R4 = Ph or arom. ring; R5 = H or lower alkyl; R3R5 or R4R5 may be linked together to form a heterocyclic ring with 3 to 7 carbon atoms; R7 = CHO, CH2OH, CO2H; X = CO, (CH2)m, SO2; Y = (CH2)m, CH2CHNHR8, CHNHR8 [R8 = lower alkyl, benzyl, R1 and R2 as described above, SOR9 where R9 = lower alkyl, C3-7 cycloalkyl, (un)substituted Ph or (un)substituted naphthyl]; R6 = (CH2)m R10 (R10 = Ph, pyridyl, thiophenyl, naphthyl, quinolinyl or C3-7 cycloalkyl); n = -1, -2, 0, 1, 2, 3, 4; m = 0, 1, 2] were prepd. as antithrombotic agents and trypsin inhibitors. Thus, Boc-L-Arg-OH.HCl (Boc = Me3CO2C) was treated with benzyl chloroformate in the presence of Et3N in THF to give 21.6% lactam II (Z = PhCH2O2C, R11 = Boc), which was Boc-deblocked by HCl in CH2Cl2 and EtOAc to give 97% II.2HCl (R11 = H). The latter was coupled with N-[3-(3-pyridyl)propanoyl]-L-proline by diphenylphosphoryl azide in the presence of Et3N in DMF to give 33% dipeptide lactam III, which was reduced by LiAlH4 in THF to give 57% arginine aldehyde IV (R12 = Z), which was Z-deblocked by hydrogenolysis over Pd/C to give IV.2HCl (R12 = H). Antithrombotic and trypsin-inhibiting activities are given for many tile compds.
IC ICM C07D401-06
ICS C07D211-76; C07K005-06; C07K005-08; C07K005-02; A61K037-64; C07D207-16; C07D409-06; C07D417-06; C07D233-88; C07D413-12
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST arginine aldehyde peptide prepn antithrombotic; trypsin inhibitor arginine aldehyde peptide
IT Anticoagulants and Antithrombotics
(arginine aldehyde-contg. peptides)
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)

(arginine aldehyde-contg., prepn. of, as antithrombotic agents)
IT 701-97-3, 3-Cyclohexylpropionic acid
RL: RCT (Reactant)
(acylation by, of arginine lactam-contg. dipeptide)
IT 3724-19-4, 3-Pyridinepropanoic acid
RL: RCT (Reactant)
(acylation by, of proline tert-Bu ester)
IT 2812-46-6, L-Proline tert-butyl ester
RL: RCT (Reactant)
(acylation of, with pyridylpropionic acid)
IT 146787-55-5 150729-30-9 150729-31-0 150729-32-1 150729-33-2
150729-34-3 150729-35-4 150729-36-5 150729-37-6 150729-38-7
150729-39-8 150729-40-1 150729-41-2 150729-42-3 150729-43-4
150729-45-6 150729-46-7 150729-50-3 150729-51-4 150729-52-5
150729-56-9 150729-57-0 150824-20-7 150824-22-9 150824-23-0
150824-25-2 150849-61-9
RL: RCT (Reactant)
(antithrombotic agent)
IT 501-53-1, Benzyl chloroformate
RL: RCT (Reactant)
(benzyloxycarbonylation by, of arginine deriv.)
IT 35897-34-8
RL: RCT (Reactant)
(benzyloxycarbonylation of)
IT 605-65-2
RL: RCT (Reactant)
(dansylation by, of dipeptide tert-Bu ester)
IT 57224-94-9
RL: RCT (Reactant)
(hydrogenolysis of)
IT 9002-07-7, Trypsin
RL: PROC (Process)
(inhibition of, by arginine aldehyde-contg. peptides)
IT 15761-39-4
RL: RCT (Reactant)
(peptide coupling of, with arginine lactam deriv.)
IT 5928-51-8P, 2-Thiophenepropanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acylation by, of proline deriv.)
IT 150728-95-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and coupling of, with arginine lactam deriv.)
IT 60189-22-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dansylation of)
IT 150728-72-6P 150728-77-1P 150728-84-0P 150728-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and de-tert-butylation of)
IT 24277-16-5P 150728-56-6P 150728-58-8P 150728-61-3P
150728-63-5P 150728-66-8P 150728-68-0P 150728-71-5P
150728-80-6P 150728-83-9P 150728-87-3P 150728-92-0P
150728-97-5P 150729-00-3P 150729-03-6P 150729-06-9P
150729-10-5P 150729-14-9P 150729-18-3P 150729-19-4P
150729-23-0P 150729-24-1P 150743-62-7P 150743-63-8P
152417-02-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deblocking of)
IT 146787-72-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydride redn. of)

IT 1124-65-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenation of)
IT 150728-55-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenolysis of)
IT 150728-94-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)
IT 150728-51-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and partial deblocking of)
IT 51219-20-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and partial deblocking-cyclization of)
IT 150728-53-3P 150728-73-7P 150728-78-2P 150728-85-1P
150728-90-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and peptide coupling of, with arginine lactam deriv.)
IT 144206-50-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and peptide coupling reactions of)
IT 150728-76-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with isothiourea deriv.)
IT 146787-68-0P 146787-70-4P 146787-71-5P 146787-73-7P
146787-74-8P 150728-60-2P 150728-70-4P 150728-74-8P
150728-79-3P 150728-82-8P 150728-86-2P 150728-91-9P
150728-96-4P 150728-99-7P 150729-02-5P 150729-07-0P
150729-09-2P 150729-13-8P 150729-17-2P 150729-22-9P
150743-61-6P 150824-19-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
IT 150728-52-2P 150728-75-9P 150729-08-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 131234-93-0P 146763-81-7P 146787-51-1P 146787-56-6P
146787-57-7P 146787-59-9P 146787-60-2P 150728-57-7P
150728-59-9P 150728-62-4P 150728-64-6P 150728-65-7P
150728-67-9P 150728-69-1P 150728-81-7P 150728-88-4P
150728-93-1P 150728-98-6P 150729-01-4P 150729-04-7P
150729-05-8P 150729-11-6P 150729-12-7P 150729-15-0P
150729-16-1P 150729-20-7P 150729-21-8P 150729-25-2P
150729-26-3P 150729-27-4P 150729-28-5P 150729-29-6P
150729-44-5P 150729-47-8P 150729-48-9P 150729-49-0P
150729-53-6P 150729-54-7P 150729-55-8P 150729-58-1P
150743-64-9P 150824-21-8P 150824-24-1P 150850-43-4P
150850-44-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antithrombotic agent)
IT 59867-91-3DP, peptides contg.
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antithrombotic agents)
IT 37980-29-3
RL: RCT (Reactant)
(reaction of, with Et bromoacetate)
IT 105-36-2, Ethyl bromoacetate
RL: RCT (Reactant)
(reaction of, with aminodiphenylimidazole)
IT 25508-20-7

RL: RCT (Reactant)
(reaction of, with dipeptide tert-Bu ester)

L17 ANSWER 31 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 119:139787 MARPAT
TI Pharmacologically active hydrazine derivatives, useful as antiviral peptide analogs, and process for their preparation
IN Faessler, Alexander; Bold, Guido; Lang, Marc; Schneider, Peter
PA Ciba-Geigy A.-G., Switz.
SO Eur. Pat. Appl., 106 pp.
CODEN: EPXXDW
PI EP 521827 A1 930107
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE
AI EP 92-810490 920625
PRAI CH 91-1962 910703
DT Patent
LA German
AB Approx. 70 hydrazine-based peptide analogs R1R2NCR3R4CR5R6CH2NR7NR8R9 [I; R1, R9 = H, acyl, (un)substituted alkyl, alkenyl, or alkynyl, heterocyclyl, (un)substituted sulfamoyl, etc.; both R1 and R9 .noteq. H; R2, R8 = H, groups listed for R1; or NR1R2, NR8R9 = heterocyclyl; R3, R4 = H, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, (un)substituted alkenyl; or R3R4 = alkylene, alkylidene, benzo-condensed alkylene; R5 = OH, R6 = H; or R5R6 = oxo; R7 = (un)substituted (cyclo)alkyl, aryl, heterocyclyl, (un)substituted alkenyl] were prepd. as inhibitors of viral aspartate proteases. For example, reaction of (2R)-[1(S)-Boc-amino-2'-phenylethyl]oxirane with tert-Bu 3-benzylcarbazate, deprotection of the product with HCl in dioxane, double coupling with Boc-Val-OH, and deprotection again gave H-Val-(S,S)-NHCH(CH2Ph)CH(OH)CH2N(CH2Ph)NH-Val-H as the tri-HCl salt. I inhibited the activity of HIV-1 and HIV-2 gag-proteases at 10-6 to 10-9 M in 2 described tests (no specific data).
IC ICM C07C243-12
ICS C07C243-24; C07C243-34; C07C271-12; C07C281-02; C07D295-182; C07D213-56; C07D215-48; A61K031-175; A61K031-395; C07D257-04; C07D213-36; C07D265-30; C07D307-12; C07D295-185
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7
ST hydrazine peptide analog prepn antiviral; HIV aspartate protease inhibitor hydrazine
IT Virucides and Virustats
(hydrazine peptide analogs)
IT Acquired immune deficiency syndrome
(treatment of, hydrazine peptide analogs for)
IT Virus, animal
(human immunodeficiency 1, infection by, treatment of, hydrazine peptide analogs for)
IT Virus, animal
(human immunodeficiency 2, infection by, treatment of, hydrazine peptide analogs for)
IT 144114-21-6, Retropepsin
RL: RCT (Reactant)
(gag, of HIV-1 and HIV-2, inhibitors of, hydrazine peptide analogs as)
IT 41153-30-4P 82527-47-7P 126410-30-8P 135544-90-0P 142526-85-0P 142526-86-1P 143185-09-5P, 4-Thiomorpholinecarbonyl chloride 144164-04-5P 149267-55-0P 149267-56-1P 149267-57-2P 149267-58-3P 149267-59-4P 149267-60-7P 149267-61-8P 149267-62-9P 149267-63-0P 149267-64-1P 149267-65-2P

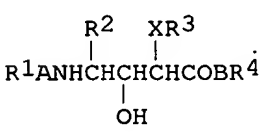
149267-66-3P 149267-67-4P 149267-68-5P 149267-69-6P
149267-70-9P 149267-71-0P 149267-72-1P 149267-73-2P
149267-74-3P 149267-75-4P 149267-76-5P 149267-77-6P
149267-78-7P 149267-79-8P 149267-80-1P 149267-81-2P
149267-82-3P 149267-83-4P 149267-84-5P 149267-85-6P
149267-86-7P 149267-87-8P 149267-88-9P 149267-89-0P
149267-90-3P 149267-91-4P 149267-92-5P 149267-93-6P
149267-94-7P 149267-95-8P 149267-96-9P 149267-97-0P
149267-98-1P 149267-99-2P 149268-00-8P 149268-01-9P
149268-02-0P 149268-03-1P 149268-04-2P 149268-05-3P
149268-06-4P 149268-07-5P 149268-08-6P 149268-09-7P
149268-10-0P 149268-11-1P 149268-12-2P 149268-13-3P
149268-14-4P 149268-19-9P 149268-20-2P 149296-81-1P
149296-82-2P 149296-83-3P 149296-84-4P 149296-85-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, as intermediate for antiviral peptide analogs)

IT 149266-91-1P 149266-92-2P 149266-93-3P 149266-94-4P
149266-95-5P 149266-96-6P 149266-97-7P 149266-98-8P
149266-99-9P 149267-00-5P 149267-01-6P 149267-02-7P
149267-03-8P 149267-04-9P 149267-05-0P 149267-06-1P
149267-07-2P 149267-08-3P 149267-09-4P 149267-10-7P
149267-11-8P 149267-12-9P 149267-13-0P 149267-14-1P
149267-15-2P 149267-16-3P 149267-17-4P 149267-18-5P
149267-19-6P 149267-20-9P 149267-21-0P 149267-22-1P
149267-23-2P 149267-24-3P 149267-25-4P 149267-26-5P
149267-27-6P 149267-28-7P 149267-29-8P 149267-30-1P
149267-31-2P 149267-32-3P 149267-33-4P 149267-34-5P
149267-35-6P 149267-36-7P 149267-37-8P 149267-38-9P
149267-39-0P 149267-40-3P 149267-41-4P 149267-42-5P
149267-43-6P 149267-44-7P 149267-45-8P 149267-46-9P
149267-47-0P 149267-48-1P 149267-49-2P 149267-50-5P
149267-51-6P 149267-52-7P 149267-53-8P 149267-54-9P
149268-18-8P 149296-76-4P 149296-77-5P 149296-78-6P
149296-79-7P 149296-80-0P 149342-91-6P 149342-92-7P
149342-93-8P 149403-90-7P 149403-91-8P 149403-92-9P
149865-19-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiviral)

IT 72-18-4, L-Valine, reactions 75-44-5, Carbonic dichloride
93-10-7, Quinoline-2-carboxylic acid 96-81-1, N-Acetylvaline
105-07-7, 4-Cyanobenzaldehyde 123-72-8, n-Butanal 123-90-0,
Thiomorpholine 407-25-0, Trifluoroacetic anhydride 459-57-4,
p-Fluorobenzaldehyde 501-81-5, 3-Pyridylacetic acid 543-27-1,
Isobutyl chloroformate 725-67-7, N-Phenylacetyl-L-valine
870-46-2, tert-Butyl carbazate 1132-68-9 1149-26-4 1685-33-2,
Z-D-Val-OH 1738-76-7, Glycine benzyl ester 4-toluenesulfonate
2038-03-1, N-(2-Aminoethyl)morpholine 2043-61-0,
Cyclohexylcarboxaldehyde 2344-80-1, (Chloromethyl)trimethylsilane
2462-34-2, Valine benzyl ester hydrochloride 3077-46-1,
N-Acetyl-L-isoleucine 3160-59-6 3256-57-3 3731-51-9,
2-Picolylamine 5891-45-2, Z-Glutamic acid tert-butyl ester
7143-01-3, Methanesulfonic acid anhydride 13211-31-9, L-Valine
tert-butyl ester 13518-40-6, Valine tert-butyl ester hydrochloride
13734-41-3 15159-40-7, Morpholinocarbonyl chloride 16652-76-9,
Valine benzyl ester 4-toluenesulfonate 24424-99-5, Boc anhydride
53370-84-6, tert-Butyl 3-benzylcarbazate 57699-53-3, tert-Butyl
3-isobutylcarbazate 66605-57-0 74761-42-5, N-Methoxycarbonyl-L-
valine 82527-46-6 92614-86-3, 3-(1-Tetrazolyl)propionic acid
98760-08-8 103495-93-8 144163-45-1 149268-15-5 149268-16-6,

(.+-.)-Isopropylmalonic acid monomethyl ester
RL: RCT (Reactant)
(reaction of, in prepn. of antiviral peptide analogs)
IT 78169-47-8, Aspartate protease
RL: RCT (Reactant)
(viral, inhibitors of, hydrazine peptide analogs as)

L17 ANSWER 32 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 119:73121 MARPAT
TI 4-amino-3-hydroxycarboxylic acid derivatives
IN Billich, Andreas; Charpiot, Brigitte; Lehr, Philip; Scholz, Dieter
PA Sandoz Ltd., Switz.; Sandoz-Patent-G.m.b.H.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
PI WO 9301166 A1 930121
DS W: AU, CA, CS, FI, HU, JP, KR, NO, PL, RO, RU, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
AI WO 92-EP1471 920630
PRAI GB 91-14261 910702
GB 91-23721 911107
GB 92-3884 920224
DT Patent
LA English
GI



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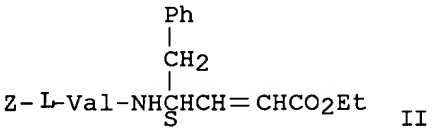

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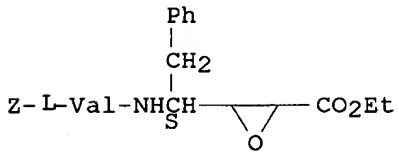
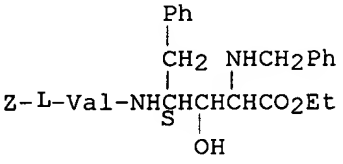


III



IV

AB Title compds. I [A and B = bond or (un)substituted amino acid residue; R1 = H, amino protecting group, R6Y (R6 = H, alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, etc.; Y = CO, NHCO,NHCS, SO2, OCO, OCS); R2 = amino acid side chain, alkyl, aralkyl, trimethylsilylmethyl, 2-thienylmethyl, etc.; R3 = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, etc.; R4 = OR7 or NHR7 where R7 has the meaning indicated for R6; X = S or NR5 (R5 = H, Me, HCO, Ac) were prepd. antiviral agents, particularly HIV-1 proteinase inhibitors. Thus, Z-L-Val-OC6H4NO2-p (Z = PhCH2O2C) was coupled with L-phenylalaninol (Phe-ol) in the presence of Et3N in DMF to give Z-L-Val-L-Phe-ol, which underwent the Swern oxidn. with oxalyl chloride and DMSO to give the aldehyde, which underwent the Wittig reaction with Ph3P:CHCO2Et in toluene to give alkene II, which underwent epoxidn. with m-chloroperbenzoic acid in CH2Cl2 to give epoxide III. The epoxide of III was cleaved by PhCH2NH2 to give title compd. IV. I were measured for their ability to inhibit HIV proteinase and to inhibit the cellular HIV-induced cytopathic effect.

Searcher : Shears 308-4994

IC ICM C07C271-22
ICS A61K031-325; C07K005-02; C07C237-22; A61K037-02
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST carboxylic acid amino hyhdroxy; hydroxy amino acid prepn antiviral; pseudopeptide prepn antiviral HIV proteinase inhibitor; human immunodeficiency virus proteinase inhibitor pseudopeptide
IT Virucides and Virustats
(pseudopeptides)
IT Virus, animal
(human immunodeficiency, proteinase of, inhibition of, by pseudopeptides)
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(pseudo-, prepn. of, as HIV proteinase inhibitor)
IT 1099-45-2
RL: RCT (Reactant)
(Wittig reaction of, with dipeptide aldehyde deriv.)
IT 102185-35-3
RL: RCT (Reactant)
(amidation of, with benzylamine)
IT 3182-95-4, L-Phenylalaninol
RL: RCT (Reactant)
(coupling of, with valine deriv.)
IT 100-46-9, Benzylamine, reactions 61671-44-1
RL: RCT (Reactant)
(epoxide ring cleavage by)
IT 9001-92-7, Proteinase
RL: PROC (Process)
(of HIV, inhibition of, by pseudopeptides)
IT 49706-31-2 80152-39-2 120369-25-7 136465-98-0
RL: RCT (Reactant)
(peptide coupling of, with pseudopeptide)
IT 10512-93-3
RL: RCT (Reactant)
(peptide coupling reactions of)
IT 148743-45-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deblocking of)
IT 148743-25-3P 148743-26-4P 148743-27-5P 148743-28-6P
148743-29-7P 148743-30-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and epoxide ring cleavage of)
IT 148743-44-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and epoxidn. of)
IT 148743-43-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sequential Swern oxidn. and Wittig reaction of)
IT 148741-78-0P 148741-79-1P 148741-80-4P 148741-81-5P
148741-82-6P 148741-83-7P 148741-84-8P 148741-85-9P
148741-86-0P 148741-87-1P 148741-88-2P 148741-89-3P
148741-90-6P 148741-91-7P 148741-92-8P 148741-93-9P
148741-94-0P 148741-95-1P 148741-96-2P 148741-97-3P
148741-98-4P 148741-99-5P 148742-00-1P 148742-01-2P
148742-02-3P 148742-03-4P 148742-04-5P 148742-05-6P
148742-06-7P 148742-07-8P 148742-08-9P 148742-09-0P
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148742-14-7P 148742-15-8P 148742-16-9P 148742-17-0P
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4-9P 148742-75-0P 148742-76-1P 148742-77-2P 148742-78-3P
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148743-03-7P 148743-04-8P 148743-05-9P 148743-06-0P
148743-07-1P 148743-08-2P 148743-09-3P 148743-10-6P
148743-11-7P 148743-12-8P 148743-13-9P 148743-14-0P
148743-15-1P 148743-16-2P 148743-17-3P 148743-18-4P
148743-19-5P 148743-20-8P 148743-21-9P 148743-22-0P
148743-23-1P 148743-24-2P 148772-73-0P 148772-74-1P
148772-75-2P 148811-26-1P 148811-27-2P 148811-28-3P
148811-29-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as HIV proteinase inhibitor)

IT 144006-29-1P 148743-31-1P 148743-32-2P 148743-33-3P
148743-34-4P 148743-35-5P 148743-36-6P 148743-37-7P
148743-38-8P 148743-39-9P 148743-40-2P 148743-41-3P
148743-42-4P 148743-46-8P 148811-30-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for HIV proteinase-inhibiting
pseudopeptide)

L17 ANSWER 33 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 117:20517 MARPAT
TI Use of aryl hydroxyurea compounds for the treatment of atherosclerosis
IN Garland, Lawrence George
PA Wellcome Foundation Ltd., UK
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
PI WO 9203130 A1 920305
DS W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
AI WO 91-GB1320 910802
PRAI GB 90-17351 900808
DT Patent
LA English
AB Compds. ArYQ (Ar = furyl, thienyl, pyrryl, etc.; Y = C1-10 alkylene, C2-10 alkenylene; Q = OR1NCOR2; R1 = H, C1-4 alkyl, Ar as above, etc.; R2 = H, C1-4 alkyl, NH2, etc.) or physiol. acceptable base salts or derivs. thereof are used in the manuf. of a medicament for the prophylaxis and treatment of a condition for which inhibition of oxidative modification of lipids is indicated, esp. atherosclerosis. The preferred compd. is N-hydroxy-N-(1-benzo[b]thien-2-ylethyl)urea

(I). I displayed antioxidant activity in peroxidn. of linoleic acid; the rate const. for scavenging of peroxyl radical was 0.11. Formulations for tablets and injectable solns. are presented.

IC ICM A61K031-34
ICS A61K031-38

CC 1-10 (Pharmacology)
Section cross-reference(s): 63

ST aryl hydroxyurea antioxidant lipid; atherosclerosis prophylaxis treatment aryl hydroxyurea

IT Lipids, biological studies
RL: BIOL (Biological study)
(antioxidants for, aryl hydroxyureas as, for disease prophylaxis and treatment)

IT Antioxidants
(aryl hydroxyureas as, for lipids, for disease prophylaxis and treatment)

IT Radicals, biological studies
Radicals, miscellaneous
RL: MSC (Miscellaneous)
(peroxide, scavenging of, by hydroxyurea deriv., in inhibition of lipid oxidn.)

IT Antiarteriosclerotics
(antiatherosclerotics, aryl hydroxyureas)

IT Lipoproteins
RL: BIOL (Biological study)
(low-d., peroxidn. of, inhibition of, by hydroxyurea deriv.)

IT Pharmaceutical dosage forms
(oral, aryl hydroxyureas in, as antioxidant for lipids, for disease propylaxis and treatment)

IT Pharmaceutical dosage forms
(parenterals, aryl hydroxyureas in, as antioxidant for lipids, for disease propylaxis and treatment)

IT Peroxides, biological studies
RL: BIOL (Biological study)
(radicals, scavenging of, by hydroxyurea deriv., in inhibition of lipid oxidn.)

IT Pharmaceutical dosage forms
(solns., injection, aryl hydroxyureas in, as antioxidant for lipids, for disease propylaxis and treatment)

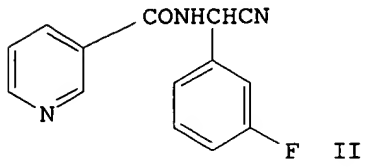
IT Pharmaceutical dosage forms
(tablets, aryl hydroxyureas in, as antioxidant for lipids, for disease propylaxis and treatment)

IT 142118-32-9
RL: BIOL (Biological study)
(as antioxidant for lipids, for disease prophylaxis and treatment)

IT 142118-32-9D, base salts 142118-32-9D, derivs.
RL: BIOL (Biological study)
(as antioxidants for lipids, for disease prophylaxis and treatment)

L17 ANSWER 34 OF 34 MARPAT COPYRIGHT 1997 ACS
AN 110:75498 MARPAT
TI Preparation of heterocyclylamidoacetonitriles as agrochemical microbicides
IN Suzuki, Hideo; Mita, Takeshi; Fukuda, Kenzo; Ochiai, Yoshinori; Hanaue, Masami; Nishikubo, Masao
PA Nissan Chemical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF

PI JP 63135364 A2 880607 Showa
AI JP 86-283881 861128
DT Patent
LA Japanese
GI



II

AB Title compds. ACONR1CR2R3CN [I; A = heterocyclyl (a no. of structures are given, e.g. pyridyl, benzopyrazolyl; dihydropyranyl, and dioxothiophenyl); R1,R2 = H, alkyl; R3 = (substituted) cyclohexyl, (substituted) Ph, (substituted) naphthalen-1- and -2-yl, (substituted) 1,2,3,4-tetrahydronaphthalen-5- and -6-yl] are prepd. by Strecker synthesis of R2R3CO with R1NH2 in the presence of KCN, followed by amidation of the resulting R1NHCR2R3CN with ACOCl. To a mixt. of NH4Cl, KCN, and 28% aq. NH3 was added a soln. of m-FC6H4CHO in PhMe at 0.degree.. stirring the resultant mixt. at room temp. overnight gave 82.0% m-FC6H4(H2N)CHCN, which was treated with nicotinic acid chloride HCl inMeCN in the presence of Et3N at 0 to room temp. to afford 77.7% a nicotinamide II, which at 500 ppm showed 100% control of Pseudoperonospora cubensis and a minor damage on cucumbers, vs. 65% for zineb. A wettable powder was formulated contg. I 25, zeeklite 69, sorpol 5039 3, and carplex 3 wt. parts.

IC ICM C07C121-47
ICS A01N037-34; A01N037-40; A01N037-48; A01N043-08; A01N043-10; A01N043-36; A01N043-40; A01N043-42; A01N043-54; A01N043-56; C07C120-00; C07C121-52; C07C121-78; C07D207-34; C07D209-08; C07D209-42; C07D213-81; C07D213-82; C07D213-89

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5, 27

ST heterocyclylamidoacetonitrile prepn agrochem microbicide; acetonitrile heterocyclylamido prepn agrochem microbicide; bactericide agrochem heterocyclylamidoacetonitrile prepn; fungicide agrochem heterocyclylamidoacetonitrile prepn

IT Amination
(Strecker, in prepn. of heterocylylamidoacetonitrile agrochem. microbicides)

IT Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
(agrochem., heterocyclylamidoacetonitriles)

IT 456-48-4P, m-Fluorobenzaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(Strecker synthesis of, in prepn. of heterocyclylamidoacetonitrile agrochem. microbicides)

IT 20260-53-1, Nicotinic acid chloride hydrochloride
RL: RCT (Reactant)
(amidation of, in prepn. of heterocyclylamidoacetonitrile agrochem. microbicides)

IT 118880-96-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of heterocyclylamidoacetonitrile agrochem microbicides)

IT 118880-32-3P 118880-33-4P 118880-34-5P 118880-35-6P
118880-36-7P 118880-37-8P 118880-38-9P 118880-39-0P
118880-40-3P 118880-41-4P 118880-42-5P 118880-43-6P
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118880-88-9P 118880-89-0P 118880-90-3P 118880-91-4P
118880-92-5P 118880-93-6P 118880-94-7P 118880-95-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as agrochem. microbicide)

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(COVERAGE TO THESE DATES IS NOT COMPLETE):
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DE 19542569 22 May 1997
EP 775693 28 May 1997
JP 09132576 20 May 1997
WO 9715580 01 May 1997

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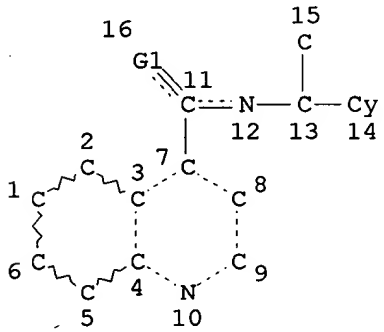
L16 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

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